

Characterization of Sleep Using Bispectral Analysis

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Abstract-This study investigated the relationship between a Bispectral Index (BIS), as measured by Aspect Medical Systems' A-1000 EEG monitor, and clinical sleep staging based on the Rechtschaffen and Kales (RK) scoring procedure. Eleven subjects - with no known sleep, respiratory, or cardiovascular disease - were tested using full polysomnography and respiratory monitoring with simultaneous recording of BIS, in an accredited sleep laboratory in Ft. Worth, Texas.

An ordinal scale was assigned to RK-based sleep stages: Wake = 1, REM = 2, Stage 1 = 3, Stage 2 = 4, Stage 3 = 5 and Stage 4 = 6. By performing linear regression between average BIS values and assigned scales, it was found that average BIS values were highly correlated with non-rapid eye movement (NREM) sleep stages and wakefulness, both within (average $R^2 \pm$ one standard deviation = 0.9376 ± 0.0264) and across subjects ($R^2 = 0.896$). However, there was a considerable amount of inter-subject variability about the average BIS value for each sleep stage. The mean BIS values for each sleep stage across all subjects were: Wake: 87.057 ± 12.967 (97.7 - 17.4); REM: 78.081 ± 10.690 (95.2 - 27.5); Stage 1: 79.452 ± 13.337 (97.7 - 25.5); Stage 2: 66.771 ± 15.493 (97.6 - 24.4); Stage 3: 41.277 ± 9.280 (87.6 - 16.9); and Stage 4: 33.832 ± 8.021 (72.3 - 13.1). Across all subjects, only the mean BIS values for REM and Stage 1 were not significantly ($P < 0.05$) different from each other. These results indicate that BIS alone may not be adequate for automated sleep staging.

Keywords ~ Sleep Staging, Bispectral Index (BIS), Rechtschaffen and Kales (RK), APAP.

I. INTRODUCTION

The amplitude and frequency of the electroencephalogram (EEG) change as a result of variation in cerebral activity between wakefulness and sleep, allowing scientists to characterize these two major functional states of the brain. Since sleep is not a homogeneous state, variations in the EEG can also be used to differentiate between the two distinct states of sleep that alternate throughout the night: non-rapid eye movement (NREM) and rapid eye movement (REM) sleep. Based on the EEG, NREM is further divided into four stages. Together, these four stages account for 80% of normal sleep time. By examining the electrooculogram (EOG) and electromyogram (EMG), REM, which may be considered the fifth stage of sleep can be identified. It accounts for the remaining 20% of total sleep time. In normal subjects NREM and REM alternate throughout the night in an approximate 90-min sleep cycle, with NREM preceding REM.

In 1968, Rechtschaffen and Kales (RK) [1] developed what has become the standard for identifying sleep stages. This method of sleep scoring relies on results obtained from the

EEG, EOG, and EMG to assign sleep to one of five stages or movement time (unscorable). Scoring of the data requires an epoch-by-epoch approach, whereby a certified scorer analyzes each 30-s epoch of data and uses subjective analysis to assign a single sleep stage score to each epoch. The RK method is labor intensive and costly, but it continues to be the standard even with automated scoring devices.

In 1996 the FDA approved the Bispectral Index (BIS) - developed by Aspect Medical Systems (Natick, MA) - as a tool for monitoring the depth of anesthesia based on advanced processing of the EEG signal. BIS was designed to provide a direct and continuous measurement of the hypnotic effects of anesthetic agents on the brain [2]. The A-1000 BIS monitor quantifies the level of hypnosis based on frequency, amplitude, and coherence of the EEG. The BIS index, on a scale of 0-100 (100 reflecting the fully conscious or awake state), is a single-number indicator of the level of induced hypnosis. Furthermore, the BIS algorithm is based on a combination of auxiliary parameters derived from a database of clinical EEG and behavioral assessment. There have been numerous reports on the efficacy of BIS in the operating room for various hypnotic agents [3,4,5]. Since patient behavior during natural sleep resembles an anesthetized patient, a few anesthesiologists have used BIS to explore its values during natural sleep [6,7].

A preliminary study by Takahashi, et al. [6] hypothesized that BIS was related to spontaneous, physiological sleep. They noticed that BIS values were high before sleep (96.4 ± 1.3), dropped immediately at the onset of sleep, and changed periodically throughout the night. They also noticed that the average BIS value was lower when the subjects woke up (93.4 ± 3.3) as compared to before they went to sleep. They suggest that the observed lower value might relate to the level of consciousness during physiological sleep.

In a more detailed study, Takahashi, et al. [7] suggested a relationship between BIS and sleep stages in man. The average BIS value varied for each sleep stage: *Wakefulness*: 93.9 ± 2.1 ; *Stage 1*: 88.3 ± 3.9 ; *Stage 2*: 80.5 ± 4.4 ; *Stage 3*: 54.96 ± 6.1 ; *Stage 4*: 40.9 ± 6.3 ; *REM*: 88.8 ± 3.8 . Average BIS values showed a decreasing trend in relation to the depth of NREM sleep. However, REM sleep was hard to identify from BIS due to its close relationship with the average BIS value for Stage 1.

Sleigh et al. [8] examined the effects of physiological sleep on BIS and then compared conventional EEG stages of sleep with changes in BIS during the first couple of hours of sleep. Sleep stages were divided into broader categories: *Wakefulness*, *Light sleep* (Stages 1 and 2), *Slow-wave sleep* (Stages 3 and 4), and *REM sleep*. Their study showed

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changes in BIS values that reflected changes in sleep architecture, and they reported average BIS values that seemed to correlate with depth of natural sleep: *Wakefulness*: 92 ± 3 , *Light sleep*: 81 ± 9 , *Slow-wave sleep*: 59 ± 10 , and *REM*: 83 ± 6 .

These studies show that changes in BIS reflect changes in sleep stages and highlight the similarities between BIS and depth of sleep. Nonetheless, previous research is limited in analysis and has not considered how well BIS correlates with conventional sleep staging, using the procedure set forth in the RK method. However, it is thought that BIS might provide an additional tool for sleep staging.

II. METHODOLOGY

Upon the approval of the Internal Human Subject Review Board of the University of Texas at Arlington, eleven adult subjects (18 years and older) - without any known history of sleep, cardiac, or respiratory disorders - were recruited to voluntarily participate in the study. There were 8 male and 3 female subjects. These subjects were 29.9 ± 8.5 years old (range: 23 - 49 years) had an average weight of 70.5 ± 9.0 kg (range: 59.9 - 80.7 kg); an average height of 1.73 ± 0.07 m (range: 1.65 - 1.85 m); and an average body mass index (BMI) of 23.4 ± 2.7 kg/m² (range: 18.2 - 27.9 kg/m²). All subjects were asked to refrain from consuming alcohol at least one week prior to their participation. Further, volunteer subjects that took any psychotropic medications were excluded from the study. Each subject was tested during an approximate 8-hour sleeping period in an accredited sleep laboratory..

BIS values, generated every 5 s by Aspect's A-1000 EEG monitor, were recorded simultaneous with standard polysomnographic data. Following each sleep study, the technical director of the sleep laboratory (blind to BIS values) scored the polysomnography data based on 30-s epochs according to the criteria set forth in the RK method.

A. Instrumentation

Fig. 1 illustrates the experimental setup used to collect BIS values and polysomnography information. BIS was derived from a bipolar EEG measured from three electrodes placed at predetermined locations on the subject's forehead (Gnd, Fpz, and At2), as shown in Fig. 2. Two EEG electrodes were used for sleep scoring based on the Modified 10-20 System of electrode placement (i.e. C3-A1 and C4-A2, not shown in Fig. 2).

B. Statistical Analysis

An ordinal scale was assigned to all sleep stages: Wake = 1, REM = 2, Stage 1 = 3, Stage 2 = 4, Stage 3 = 5 and Stage

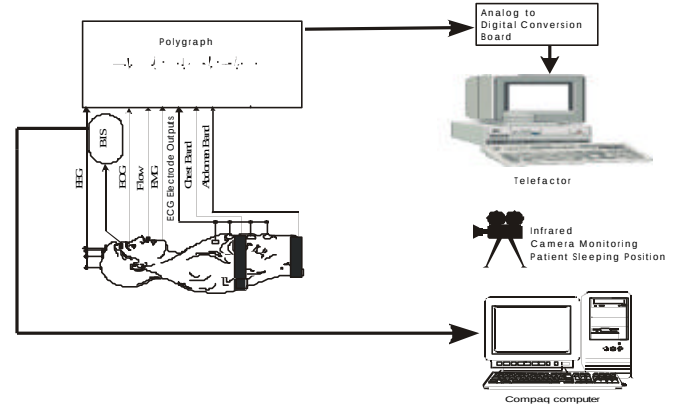


Fig. 1. Experimental setup for BIS and polysomnography data acquisition.

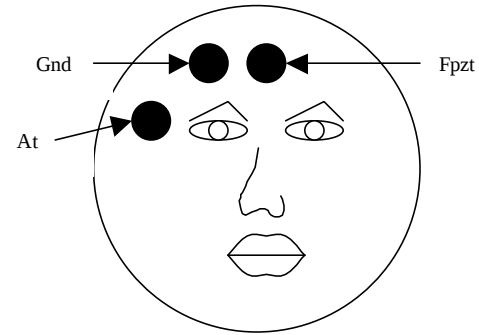


Fig. 2. Electrode montage for BIS

4 = 6, and the degree of correlation between mean BIS values and depth of NREM sleep both within and across subjects was determined from simple linear regression analysis. The proportion of the total variation in mean BIS values accounted for by the fitted regression line was determined as the coefficient of determination, R^2 . The equation used to calculate this coefficient was:

$$R^2 = \frac{\sum (\hat{Y}_i - \bar{Y})^2}{\sum (Y_i - \bar{Y})^2} \quad (1)$$

where Y_i represents BIS values used for constructing the regression line, $\hat{Y}_i$ represents BIS values from the regression line, and $\bar{Y}$ represents the mean BIS value from Y_i values.

In addition, a mean BIS value $\pm$ one standard deviation was determined for each sleep stage and wakefulness, across all subjects.

III. RESULTS

As shown in Fig. 3 for subject #3, there were significant changes in BIS that tend to reflect the variation in depth of natural sleep and mimic classical sleep architecture. There was a high correlation between mean BIS values and depth of NREM sleep for all subjects (0.9376 ± 0.0264). The linear

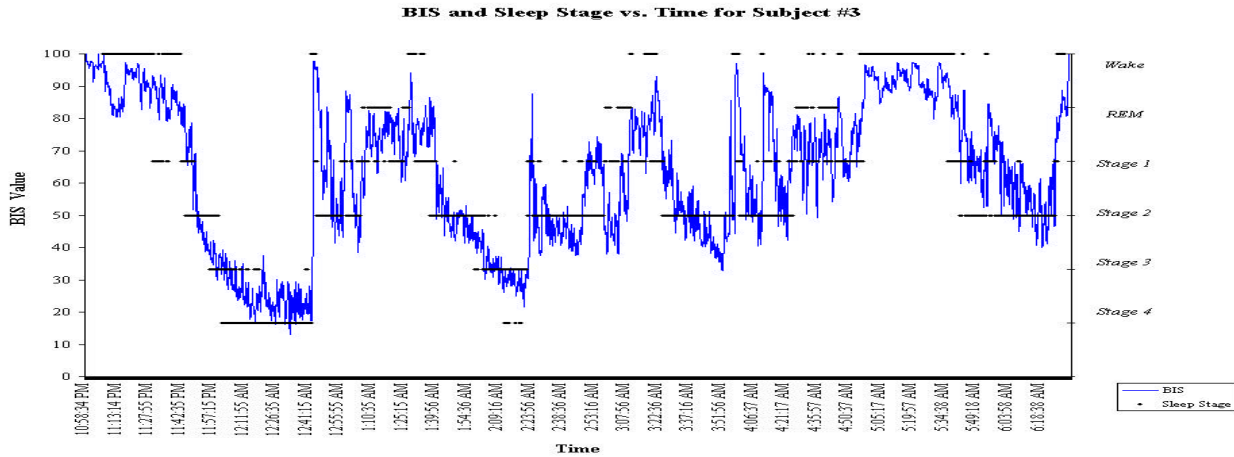


Fig.3 BIS values and sleep stage scores for subject #3

regression plot and R^2 value for subject #3 is illustrated in Fig. 4. Also, inter-subject linear regression analysis shows a high correlation between mean BIS values collected from all subjects and depth of NREM sleep ($R^2 = 0.8962$), as provided in Fig. 5. As can be seen from the results in Fig. 6, this correlation dropped ($R^2 = 0.8367$) when REM was placed

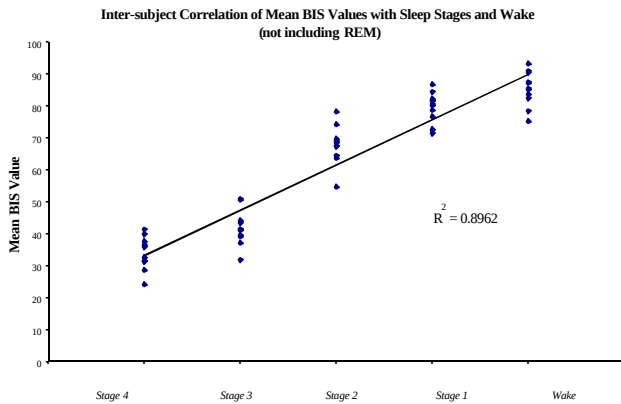


Fig. 4 Correlation between mean BIS values and depth of NREM sleep for subject #3

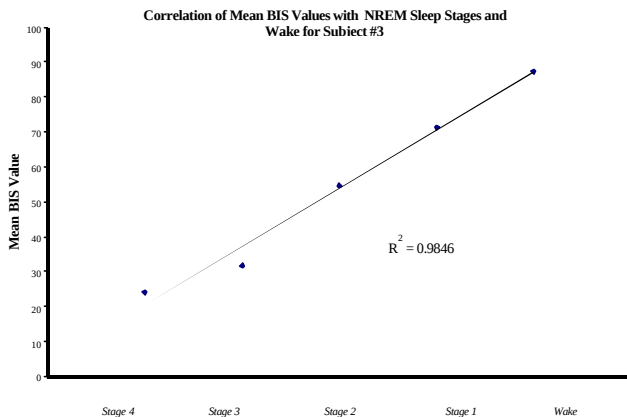


Fig. 5 Inter-subject correlation between mean BIS values and depth of NREM sleep

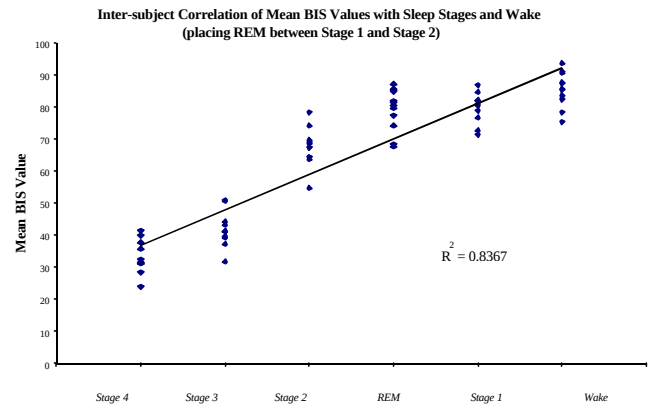


Fig. 6. Inter-subject correlation between mean BIS values and depth of sleep, by placing REM between Stages 1 and 2 of NREM

between Stage 1 and Stage 2 of NREM in the depth of sleep order.

All of the individual BIS values for each sleep stage and wakefulness, across all subjects (globally), were averaged to create the chart in Fig. 7. There was a considerable amount of inter-subject variability about the average BIS value for each sleep stage and wakefulness, as evidenced by the large interval of $\pm$ one standard deviation about each average value. The average $\pm$ one standard deviation and range (indicated in parentheses) of BIS values for each sleep stage across all subjects were: Wake: 87.057 ± 12.967 (97.7 – 17.4); REM: 78.081 ± 10.690 (95.2 – 27.5); Stage 1: 79.4 ± 13.3 (97.7 – 25.5); Stage 2: 66.8 ± 15.5 (97.6 – 24.4); Stage 3: 41.3 ± 9.2 (87.6 – 16.9); and Stage 4: 33.8 ± 8.0 (72.3 – 13.1).

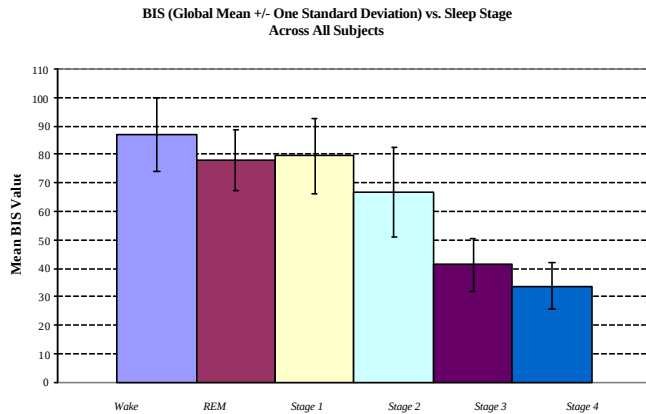


Fig. 7. Global average BIS value $\pm$ one standard deviation for each sleep stage and wakefulness

IV. DISCUSSION

Within all subjects, there is a distinctive decreasing trend in BIS values with increasing depth of sleep and an increasing trend with decreasing depth of sleep. Moreover, this trend appears to mirror the approximate 90-min sleep cycle seen in normal subjects and mimic classical sleep architecture.

The strong correlation between the mean BIS values and the ascending ordinal scale for NREM sleep stages suggests that BIS is reflective of depth of NREM sleep. This, in turn, implies that depth of physiological sleep reduces the phase coupling of the sinusoidal components present in the EEG, as lower BIS values reflect less phase coupling among the sinusoidal components. However, because the EEG during REM is similar to Stage 1 of NREM, it does not appear that BIS can distinguish between these two stages. As a consequence, a much weaker relationship is observed between average BIS values and depth of sleep when REM is included in the depth of sleep order. Higher values of BIS during REM sleep are likely to have resulted from the contamination of EEG signals sensed by the electrodes positioned near the eye (Fig. 2). Although there is a strong relationship between average BIS values and depth of NREM sleep, there is also measurable amount of variability about the average value for each sleep stage and wakefulness. Ultimately, this variability may limit the ability of BIS to significantly distinguish among all sleep stages.

V. CONCLUSION

The results of this study suggest that BIS reflects changes in the EEG that relate to natural sleep. A strong correlation between average BIS values and depth of NREM sleep both within and across subjects quantitatively supports this. BIS values associated with REM sleep do not correlate well with depth of sleep. Furthermore, the large amount of variability about the average BIS value for each sleep stage and wakefulness, limits the potential of BIS for automated sleep-staging without additional processing.

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