# The use of Bispectral Index (BIS) values as an indicator for sleep staging

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**SUMMARY.** The aim of this study was to examine whether BIS values during sleep correspond to the different sleep stages, in order to assess BIS as an alternative means of sleep staging. **Patients-Methods**: The study was conducted on 23 patients who were examined concurrently with polysomnography (PSG) for diagnosing sleep-disordered breathing and with BIS. Exclusion criteria were sleep duration <4 hours, sleep efficiency <80% on PSG and signal quality index (SQI) <50% on BIS. Comparisons in recordings were performed. **Results**: The patients provided 806 different sleep periods. The mean BIS value was 93.6±4.8 in the wakeful state, and in sleep, according to each stage: 84±11.5 in stage 1, 75.4±13.2 in stage 2, 53.4±15.8 in slow wave sleep (SWS), and 81.5±13.3 during REM sleep. A significant difference was observed between BIS values in the wakeful state and stage 1 (p<0.005) and between stages 1 and 2 and SWS (p<0.001), but not between stage 1 and REM (p=0.102). **Conclusion**: BIS values decrease with sleep and remain low, with the exception of REM sleep, the BIS values in which overlap with those in stage 1, reducing the sensitivity of BIS in sleep staging. ***Pneumon 2009, 22(3):235-239.***

## INTRODUCTION

The Bispectral Index (BIS) is a processed encephalographic (EEG) parameter used for providing a direct measure of the effects of anaesthetics and sedatives on the brain. Several studies investigating the changes in BIS values during sedation have demonstrated that BIS correlates well with various clinical hypnotic end points[1].

It has been hypothesized that BIS values decrease during natural sleep and if this is confirmed, BIS could be a useful, easy method for use in clinical sleep studies. The gold standard technique for the diagnosis of sleep apnoea and related disorders is overnight polysomnography (PSG)[2,3], but increasing attention is being paid to the development of limited diagnostic studies for use in clinical practice[4,5].

Data concerning the degree and the pattern of the reduction of BIS values during sleep are scarce and conflicting[6,7]. The aim of this study was to examine whether changes in BIS values correspond to sleep stages in individuals examined with PSG for investigation of reported breathing disorders during sleep.

## PATIENTS AND METHODS

Twenty three patients (18 males and 5 females) were enrolled in the study, all of whom had suspected sleep apnoea-hypopnea syndrome (SAHS), based on reported symptoms and clinical signs. Exclusion criteria were a history of, or current, head injury, cerebral ischaemia or other neurological disease, administration of psychotropic medication or alcohol abuse.

A clinical history was taken from each patient and daytime sleepiness was estimated using the Epworth Sleepiness Scale (ESS)[8]. All the patients underwent anthropometric measurements, spirometry by Ganshorn Medizine Electronic (GmbH) and analysis of blood gases from an arterial sample on room air (Radiometer Co). Sleep study was performed in the Sleep Unit from 23.00 pm to 6.30 am, using standard PSG. PSG variables were recorded with a computerized 16 channel recording (Embla 7000, Flaga) of electroencephalogram (EEG C4/A1, C3/A2), electrooculogram (EOG), chin electromyogram (EMG), electrocardiogram (ECG), oral and nasal flow, abdominal and thoracic movements, snoring and oxygen saturation. The recorded EEG data of each subject were analyzed manually according to standard criteria for sleep staging. Total sleep time (TST) and sleep efficiency (SE) were recorded. The sleep stages, i.e., stages 1 and 2, slow wave sleep (SWS) and rapid eye movement (REM) sleep were expressed as % of TST. The duration of wakefulness (before sleep initiation) and the awakenings between sleep stages were also measured. According to the apnoea-hypopnoea index (AHI), SAHS was classified as mild/moderate (AHI 5-30/hour) and severe (AHI >30/hour), while individuals with AHI <5/hour served as controls.

BIS electrodes were placed on the head according the manufacturer's instructions and signals were recorded with an Aspect Medical Systems A-2000 XP. The quality of the signal was expressed by signal quality index (SQI) ranging between 0-100. BIS values with SQI >50%, were included in the analysis at the end of each sleep period lasting at least 2 minutes.

### Statistical analysis

Descriptive statistics were used and comparisons between different groups were performed with analysis of variance (ANOVA). BIS values in different sleep stages were expressed as mean±standard deviation and also as median values. Statistical significance was accepted for p values <0.05.

## RESULTS

The 23 subjects in the study manifested a wide range of breathing disorders during sleep. In all of them sleep efficiency was above 80%, and TST was >4h with a normal distribution of sleep stages, although a reduction in the proportion of SWS and REM was observed. Seven individuals with AHI <5/hour served as controls. In 6 patients mild/moderate SAHS was detected (i.e., AHI 5-30/hour), while in 10 patients AHI was >30/hour, indicating severe SAHS. No difference in age distribution was observed between groups, but the duration of sleep stages showed significant differences. The anthropometric characteristics, pulmonary function and PSG results of the 23 patients are displayed in Table 1.

Only BIS values with SQI >50% were included, giving a total of 806 different sleep periods, each lasting at least 2 minutes, in different sleep stages, to be analyzed. The median BIS value during the wakeful state was 96, and a gradual decrease was observed with the appearance of sleep stage 1. The lowest BIS values were recorded during stage 2 and slow wave sleep (SWS), and the highest during stage 1, REM and in the awakenings between sleep. A statistically significant difference in BIS values was observed between the wakeful state and stage 1 (p <0.001) and between stage 1 and stage 2 and SWS; (p <0.001), but not between stage 1 and REM (p=0.102).

Table 2 displays median and mean BIS values during each sleep stage for all patients. A great variation in BIS values during all sleep stages was observed and a considerable overlap was revealed, as shown in Figure 1.

BIS values were generally low during sleep, but there was a wide variation in values and an overlap was observed between the different sleep stages (Table 3). The distribution pattern of BIS values differed between the 3 groups of patients. Patients with severe SAHS, who had the worst sleep quality, manifested a significant overlap of BIS values in stages 1, 2, REM and arousals. Figures 2, 3, and 4 show BIS values in each sleep stage in the three subgroups.

**TABLE 1.** Anthropometric characteristics and respiratory function in the wakeful state and sleep characteristics of all patients and in each subgroup separately

| | Total (n=23) | Normal (n=7) | Mild/moderate SAHS (n=6) | Severe SAHS (n=10) |
|---|---|---|---|---|
| Age (years) | 47.2±7.1 | 45.2±4.8 | 46.8±5.8 | 48.8±9.1 |
| BMI (Kg/m$^2$) | 29.5±5.8 | 28.1±3.8 | 27.5±3.2 | 31.6±7.7 |
| $FEV_1$ (%pred) | 92.0±14.5 | 93.0±7.5 | 101.2±15.6 | 85.7±15.6 |
| FVC (%pred) | 90±14.1 | 89.4±8.4 | 100.1 ±14.4 | 84.2±14.7 |
| $PAO_2$ (mmHg) | 88.5±9.3 | 88.5±10.3 | 92.7±6.6 | 86.0±9.9 |
| $PACO_2$ (mmHg) | 37.6±2.2 | 37.4±1.3 | 38.2±2.0 | 37.4±2.8 |
| ESS | 7.3±4.1 | 8.0±3.5 | 5.5±4.0 | 7.0±4.5 |
| AHI (/hour) | 25.7±24.7 | 1.9±1.3 | 11.8±7.4 | 50.6±14.3 |
| min$SpO_2$ (%) | 81.3±9.7 | 89.1±2.8 | 81.5±8.4 | 75.8±10.3 |
| SE (%TST) | 81.6±13.7 | 84.3±7.8 | 90.9±8.6 | 74.2±16.4 |
| TST (minutes) | 312.3±70.4 | 314.4±47.7 | 353.1±19.3 | 286.4±92.5 |
| S1 (%TST) | 19.2±13.7 | 17.2±17.2 | 17.5±10.5 | 21.6±13.9 |
| S2 (%TST) | 39.3±12.2 | 39.3±14.2 | 40.8±14.0 | 38.5±11.4 |
| SWS (%TST) | 12.2±7.1 | 14.1±5.6 | 19.7±4.4 | 6.7±4.3 |
| REM (%TST) | 12.3±7.3 | 15.9±6.1 | 12.7±6.8 | 9.7±7.9 |
| Awakenings | 18.4±13.7 | 15.7±8.5 | 9.0±8.7 | 25.7±16.4 |

AHI= Apnea Hypopnea Index, BMI= Body Mass Index, ESS= Epworth Sleepiness Scale, REM= Rapid Eye Movement, SE= Sleep Efficiency, SWS= Slow Wave Sleep, TST= Total Sleep Time

**TABLE 2.** Bispectral Index (BIS) values according to sleep stages

| Sleep Stage | BIS (mean±SD) | BIS (Median value) | min | max |
|---|---|---|---|---|
| Wakeful state | 93.6±4.4 | 96 | 85 | 98 |
| Stage 1 | 84.0±11.5 | 86 | 65 | 98 |
| Stage 2 | 75.4±13.2 | 79 | 34 | 98.3 |
| SWS | 53.4±15.8 | 48 | 31 | 96.6 |
| REM | 81.5±13.3 | 83 | 62 | 93 |
| Awakenings | 88.1±8.1 | 90 | 75 | 99.1 |

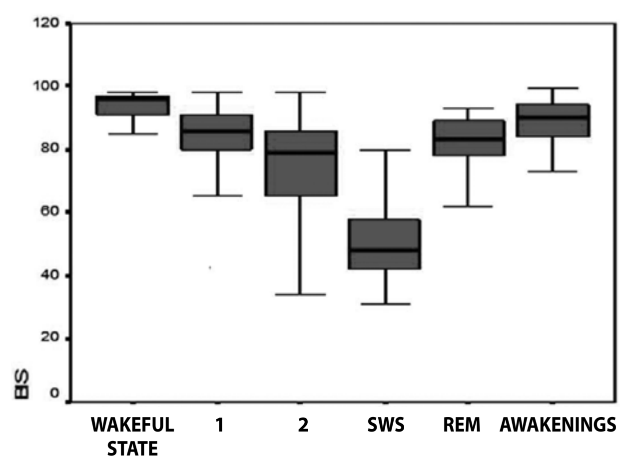


**FIGURE 1.** BIS values in different sleep stages (n= 23).

## DISCUSSION

The findings of this study, which is the first conducted to Greek patients, indicate that BIS values are sensitive in reflecting the changes in EEG sleep recordings. The BIS values decreased progressively as sleep became deeper, but they were not specific in identifying change in the sleep stages, especially in situations with disturbed sleep, which is characteristic in patients with sleep disordered breathing.

Few studies have compared BIS values with sleep processing and the results are conflicting. Sleigh et al[6] assessed the change in BIS values during sleep in a small number of healthy subjects in their homes. Although a good correlation between BIS values and the depth of sleep was revealed, comparison of measurements of BIS values during the wakeful state, stage 1 and REM sleep was confusing. BIS values during sleep in the present study are comparable to those reported by Sleigh et al,

**TABLE 3.** Bispectral Index (BIS) values in sleep stages according to severity of sleep apnoea-hypopnoea syndrome (SAHS)

| | Normal | | Mild/moderate SAHS | | Severe SAHS | |
|---|---|---|---|---|---|---|
| **Sleep stages** | **mean±SD** | **Median** | **mean±SD** | **Median** | **mean±SD** | **Median** |
| Wakeful state | 95.6±2.7 | 97 | 91.6±2.5 | 92 | 92.0±4.8 | 93 |
| Stage 1 | 86.4±9.4 | 89.5 | 92.3±2.6 | 92.5 | 87.3±6.5 | 89 |
| Stage 2 | 78.4±12.8 | 81 | 77.1±15.0 | 82 | 78.9±12.1 | 82 |
| SWS | 43.2±8.0 | 44.5 | 56.4±14.8 | 56 | 60.5 ±18.1 | 56 |
| REM | 85.4±7.1 | 92 | 83.6±14.5 | 88 | 81.3 ±8.0 | 82.5 |
| Awakenings | 90.3±6.4 | 85 | 84.2±14.9 | 90 | 86.6±7.6 | 88 |

SWS = slow wave sleep, REM = rapid eye movement

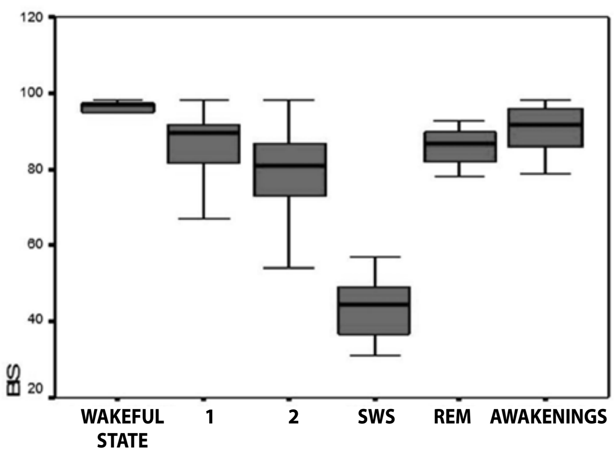


**FIGURE 2.** BIS values in different sleep stages in the control group (AHI<5/hour) (n=7).

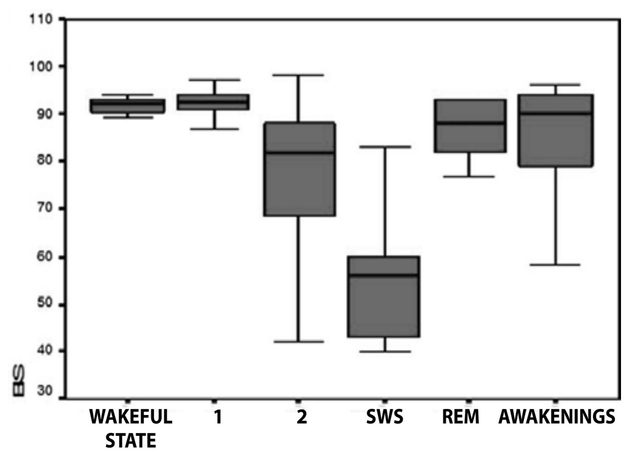


**FIGURE 3.** BIS values in different sleep stages in patients with mild/moderate SAHS (n=6).

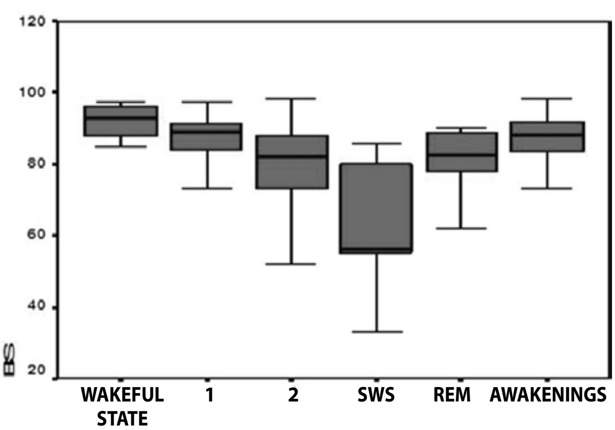


**FIGURE 4.** BIS values in different sleep stages in patients with severe SAHS (n=10).

but they overlap significantly between different sleep stages, making the distinction of sleep stages difficult. The overlap was more pronounced between sleep stage 1, REM sleep and the awakenings. Nieuwnhuijs et al[7] reported BIS values which were low during sleep, with even lower values observed during REM sleep, and they concluded that BIS cannot be used as an accurate predictor of sleep process due to the wide spread of values during sleep.

The results of the present study confirm this conclusion, although BIS values were found to be higher in all sleep stages, and especially in REM sleep, than those of the aforementioned study. The present study included a larger number of patients suspected to have SAHS, which enabled comparisons between subgroups according to severity. As is well known, sleep quality is poor in SAHS patients, with awakenings and arousals from sleep and frequent shifts of stages, which provided a good test of the efficacy of BIS.

It was concluded that BIS values were low during sleep in patients with SAHS, as well as in the individuals with AHI<5/hour. Still, it was observed that the pattern of BIS variance was different between different groups of patients.

Nicholson et al[9], who studied 27 adult ICU patients using BIS with the supplementary use of submental EMG, reported a cyclical sleep pattern in half of them approaching the normal sleep pattern. Benini et al[10] reported that in normal children BIS values correlated well with EEG recorded sleep stages. Unfortunately, an important limitation to their study was the failure to record REM sleep.

In conclusion, BIS values are lower during sleep, as they are during sedation, but the pattern of reduction is not sufficiently accurate to predict sleep stages. Most importantly, BIS is not able to distinguish awakenings from REM sleep, probably due to the EEG pattern in REM sleep which is very similar to that in stage 1 and in the wakeful state.

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