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## Research Article

# Correlation between Bispectral Index and Sleep Stage of Patients with Obstructive Sleep Apnea-Hypopnea Syndrome

### Abstract

**Objective:** The aim of this study was to evaluate the correlation between bispectral indexes (BIS) and sleep staging in patients with moderate to severe obstructive sleep apnea-hypopnea syndrome (OSAHS) under natural sleep conditions.

**Materials and Methods:** Twelve patients who had been clinically diagnosed with OSAHS were monitored by polysomnography (PSG) and bispectral index (BIS) that were simultaneously recorded to determine the BIS at different sleep stages and analyze the patterns.

**Results:** One patient did not meet the diagnostic criteria of OSAHS, and another patient lacked non-rapid eye movement stage 3 (N3) during sleep. Both patients were excluded from this study. Ten patients who met the diagnostic criteria of moderate to severe OSAHS were included in the final statistical analysis. The BIS during the following sleep stages, i.e., awake, stages N1, N2, N3, and rapid eye movement (REM) ranged from 75-91, 65-91, 60-86, 47-82, and 66-91, respectively (mean  $\pm$  standard deviation: 86.3  $\pm$  4.62, 78.4  $\pm$  9.72, 73.8  $\pm$  8.59, 61.8  $\pm$  11.90, and 83.3  $\pm$  7.32, respectively).

**Conclusion:** BIS gradually decreased in the deeper stages of sleep. However, there was a considerable overlap in BIS values between different sleep stages, making it difficult to use BIS as a marker for sleep staging. To ensure an accurate examination of airways in the patient during sleep induction, these should be executed when the BIS is reduced to 77 or below.

## Introduction

Obstructive sleep apnea-hypopnea syndrome (OSAHS) refers to apnea and inadequate ventilation caused by collapsing upper airways and is associated with snoring, sleep disorders, frequent oxygen desaturation during sleep, and excessive daytime sleepiness [1,2]. Stenosis or occlusion of the upper respiratory tract during sleep is the main reason for the occurrence of OSAHS [3]. Surgery is one of the effective treatment options for OSAHS by preventing the stenosis or occlusion of the upper respiratory tract. Accurate diagnosis of the stenosis or occlusion of the upper respiratory tract is the key for selection of a surgical treatment approach and its efficacy [4].

In addition to a series of examinations when the patient is awake [5,6], a number of examinations during natural sleep conditions and after sleep-induction have been widely used in recent years to locate the stenosis and occlusion of upper respiratory tract accurately [7-10]. Specifically, drug-induced sleep endoscopy (DISE) is a commonly used technique to examine the upper respiratory tract during sleep. DISE directly identifies the morphological changes in the various parts of the upper respiratory tract during apnea, thereby confirming the site of obstruction in the airway [11-14]. DISE is an important and significant diagnostic tool guiding the surgical treatment and helping select an appropriate operative plan [15]. DISE has been widely used as a routine clinical screening tool.

Even with the advancement of examination equipment and skills, patients should reach a certain depth of sleep during the examination to ensure accurate and reliable examination results. Variations in the depth of sleep can result in different examination results [16]. Although electroencephalography or polysomnography can accurately determine the depth of sleep in the patients, the machines cannot be conveniently placed and used in operating rooms, where most sleep-inducing examinations are performed. Most physicians use BIS to monitor the depth of sedation during DISE [13-15]. However, to date, only one study has reported on the correlation between BIS and sleep stage in mild OSAHS patients [17]. Patients with moderate to severe OSAHS often have sleep structure disorders. However, regarding the correlation between BIS and sleep stage, we do not know if there are any differences among healthy adults, and patients with mild, moderate or severe OSAHS. This study was conducted in a group of patients with moderate to severe OSAHS using PSG with simultaneous recording of BIS of each patient to evaluate the relationship between BIS and sleep stages.

## Materials and Methods

### Research subjects

This study was approved by the Ethics Committee of our hospital. Twelve consecutive patients were suspected of OSASH and scheduled to be examined by PSG in our hospital during March

2015. All patients signed the written informed consents prior to the participation of PSG and BIS monitoring. PSG confirmed moderate to severe OSAHS in patients and all components of the sleep stages were included in this study.

### PSG for sleep apnea and sleep staging

In this study, PSG using Respironics ALICE<sup>5</sup> Diagnostic Sleep System (Philips Healthcare, Andover, MA) was performed for sleep monitoring in all patients via the 10-20 neural input layout connecting to the heads of patients. Electroencephalogram (EEG), electrooculogram (EOG), and electromyogram (EMG) activities of frontal, parietal, and occipital regions in each patient were monitored. The obtained sleep electroencephalograms were used to interpret the sleep stages according to *the American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events* published in 2007 [18]. This manual divides sleeping into several stages, including wakefulness (W), non-rapid eye movement 1 (N1), non-rapid eye movement 2 (N2), non-rapid eye movement 3 (N3), and rapid eye movement (REM). Nasal air pressure and flow, thermal airflow, snoring, chest and abdominal movements, posture, electrocardiogram (ECG), activity of lower extremity EMG, and blood oxygen saturation were measured simultaneously. In addition, interpretation of respiratory events was based on the same rule to determine the apnea hypopnea index (AHI) and the lowest oxygen saturation during sleep as the primary diagnostic indicators of OSAHS. Diagnostic criteria of OSAHS were confirmed when AHI reached or exceeded 5 times per hour (mild OSAHS: AHI < 15 times/h; moderate OSAHS: 15-29.99 times/h; severe OSAHS: 30 times/h).

### BIS recording

All patients underwent PSG and BIS (BIS-Vista, Aspect Medical System, Newton, MA) monitoring simultaneously according to the methods described previously in the literature [19]. The methods are summarized as follows: BIS system clock and PSG system was synchronized before the examination. After the patient's skin had been cleaned, the supporting BIS electrode strips were installed according to the manufacturer's instructions. Electrodes were located on the forehead, on the right orbit, between the right preauricular region and the right lateral cheekbone. The high-pass and low-pass filters of EEG were set to 0.5 Hz and 30 Hz, respectively. The signal quality index (SQI) was >95%, and the electrode impedance was <5 kΩ. After the machine had passed the self-examination, BIS system continuously recorded EEG activities and automatically converted the data into BIS. The BIS values were stored automatically in the system every minute.

### Data processing and statistical analysis

After overnight monitoring, the sleep stages were determined according to PSG data recorded in 30-second intervals throughout the night and the corresponding BIS values were recorded. The BIS values during sleep stages (e.g., W, N1, N2, N3, and REM) were recorded throughout the night from the same patient and the mean BIS was calculated for each sleep stage. The mean BIS of individual patients at different sleep stages were included in the final statistical analysis. SPSS 17.0 statistical software was used for data processing.

BIS at different sleep stages of all patients were used for descriptive statistics. ANOVA analysis was used to explore the differences between the sleep stages. Rank correlation analysis was performed between BIS and different sleep stages.

## Results

### Patients

Twelve patients who consecutively visited our hospital participated in this study. Their PSG and BIS were monitored simultaneously. One of the PSG results did not meet the diagnostic criteria of OSAHS, and the patient was excluded. Another patient without N3 sleeping component throughout the night was also excluded from the study. Ten patients with moderate to severe OSAHS were included in the statistical analysis (8 males and 2 females; age ranged 19–48 years; mean age  $33.1 \pm 10.72$  years), with 3 cases of moderate OSAHS and 7 cases of severe OSAHS; AHI ranged 17.8–98.0 times/h (average:  $49.1 \pm 31.92$  times/h); L<sub>Sa</sub>O<sub>2</sub> 0.58–0.90 (average:  $0.75 \pm 0.12$ ); BMI ranged from 21.0–44.1 kg/m<sup>2</sup> (average:  $29.5 \pm 5.93$  kg/m<sup>2</sup>); and Epworth Sleepiness Scale ranged 2–21 scores (average:  $12.4 \pm 4.37$  scores). All patients were snoring throughout the night. The severity of excessive daytime sleepiness and fatigue varied from case to case.

### Sleep quality

Ten OSAHS patients successfully completed PSG and BIS monitoring. All patients had basal stages of W, N1, N2, N3, and REM throughout the night. Table 1 shows the time distributions of different sleep stages.

### BIS analysis in different sleep stages

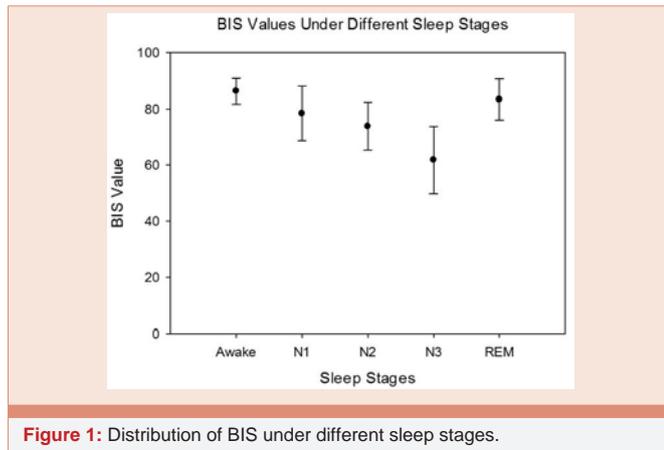
Table 2 and Figure 1 shows the BIS distribution of 10 patients in different sleep stages. Mean BIS values gradually decreased from W to N3 stages. ANOVA showed significant differences of BIS among all sleep stages (F value: 11.789, P < 0.001). Rank correlation analysis

**Table 1:** Time distribution of different sleep stages in OSAHS patients through the night (minutes).

	Minimum value	Maximum value	Mean	Standard deviation
Total awake time	7	61	26	17.9
Total sleep time	213	368	296.3	52.4
Stage N1 Time	4	67	40.6	19.7
Stage N2 time	56	204	134.2	60.4
Stage N3 time	12	120	55.6	34.9
Rapid eye movement (REM) time	11	174	43.2	48.3

**Table 2:** Distribution of BIS under different sleep stages.

BIS	Minimum value	Maximum value	Mean	Standard deviation
Awake	75	91	86.30	4.62
Stage N1	65	91	78.40	9.72
Stage N2	60	86	73.80	8.59
Stage N3	47	82	61.78	11.90
Rapid eye movement (REM)	66	91	83.34	7.32



**Figure 1:** Distribution of BIS under different sleep stages.

between BIS and sleep stages of W, N1, N2, and N3 demonstrated a significant correlation (correlation coefficient: 0.699,  $P < 0.001$ ).

## Discussion

BIS is an indexed number that integrates complex information and is derived from fast Fourier transformation and bispectral analysis of the power and frequency data of EEG. BIS represents the functional status of the cerebral cortex and indicates the sedation level. It is usually used for monitoring the depth of anesthesia on a numerical range from 0 to 100, with larger values indicating a lower depth of anesthesia and smaller values indicating deeper anesthesia [20]. Studies have shown a correlation between BIS and sleep stages during natural sleep in healthy adults and children [21,22], confirming that BIS gradually declines with increasing depth of sleep. This also suggested that BIS reflected the awareness level of the tested subject to a certain degree.

For patients with moderate to severe OSAHS who are unable or unwilling to receive treatment with positive pressure ventilation, surgery is an alternative treatment. DISE is a common method to locate the suiTable airway obstruction site for surgery [11,12]. During the DISE for airway evaluation, most researchers use the BIS system to monitor the sedation level of OSAHS patients [13-15]. However, to date, no study has reported the correlation between BIS and sleep stages under natural sleep in patients with moderate to severe OSAHS. Here, we monitored the PSG and recorded BIS in the same group of OSAHS patients to understand the relationship between BIS and different sleep stages of the OSAHS patients.

Among the selected cases, we excluded patients who did not meet the diagnostic criteria (i.e., standard snoring case, mild OSAHS case, and case with incomplete sleep stages) for OSAHS. Although the sample size in this study was small ( $n = 10$  cases), all patients experienced all sleep stages (W, N1, N2, N3, and REM stages), which were used to summarize the regular patterns between accurate sleep staging and BIS.

As shown in Table 2 and Fig 1, the BIS distribution during the different sleep stages of the 10 patients showed that the mean BIS gradually decreased from W to the N3 stages. ANOVA showed significant differences between BIS at different sleep stages (F value:

11.789,  $P < 0.001$ ). Rank correlation analysis between BIS and sleep stages W, N1, N2, and N3 demonstrated a significant correlation (correlation coefficient: 0.699,  $P < 0.001$ ). These findings were similar to the correlation studies between BIS and sleep stages during natural sleep in healthy adults and children [21,22], thereby confirming that BIS gradually declines with increasing depth of sleep. BIS reflected the awareness level of the tested subjects to a certain degree.

Although an increasing depth of sleep was associated with gradual reduction of BIS (Table 2, Figure 1), many overlapping scores were found between different sleep stages. Therefore, it was difficult to solely rely on BIS to distinguish different sleep stages in OSAHS patients clearly. This result was similar as the findings in healthy adults [19,21]. Evidence has shown that increasing depth of sleep significantly increased the frequency and severity of respiratory problems. DISE results were significantly affected by the depth of sedation [16]. This suggested that a fixed sedation level should be used during DISE. Although BIS could not be used to distinguish different sleep stages, monitoring of BIS during DISE to ensure that DISE was performed under the same level of BIS during each examination remains a recommended practice.

Although the number of subjects in this study is small and BIS cannot distinguish different sleep stages, we still try to recommend a cut-off value for BIS under DISE. Of the 10 OSAHS patients in this study, the mean BIS of the W stage was 86.3, with a standard deviation of 4.62 and a lower limit of the 95% confidence interval of 77.24, thereby suggesting that 95% of the OSAHS patients entered the sleep state when  $BIS < 77.24$ . The most basic requirement of DISE is to ensure that the tested subject enters the sleep state before preceding any examination. Hence, we proposed to use BIS system in DISE to monitor the depth of sedation. The corresponding examination should be initiated when  $BIS < 77$  to ensure the patient has entered in the sleep state. The same BIS level should be used during each examination to allow the comparability of examination results in different cases or for the same case at different time points.

Finally, only natural sleep-wake states/stages were evaluated in this study, The EEG activity and BIS are likely to differ between natural and drug-induced sleep, and we will continue to observe the correlation between sleep stages and BIS in drug-induced sleep states.

## Conclusion

Similar to healthy adult and patients with mild disease, BIS gradually decreases during deeper stages of sleep in patients with moderate and severe OSAHS. In addition, there was also a considerable overlap in BIS values between different sleep stages, making it difficult to use BIS as a marker for sleep staging. To ensure an accurate examination of the airways in patient during sleep induction, these should be executed when the BIS is reduced to 77 or below.

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