

Sleep Patterns in Intensive Care Unit Patients: A Study Using the Bispectral Index

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ABSTRACT

Objective: *To objectively record sleep patterns in intensive care unit patients using the Bispectral Index as an electroencephalographic measure of sleep and to determine if the sleep pattern is correlated with various clinical factors.*

Methods: *Adult intensive care patients were recruited who were in the recovery phase of their illness and on minimal sedation. The sleep pattern was examined using an overnight recording of the patient's Bispectral Index and submental electromyogram.*

Results: *Twenty-seven adult patients in a tertiary level general intensive care unit were enrolled. The sleep pattern was examined using an overnight recording of the patient's Bispectral Index and submental electromyogram. No intensive care unit patients showed a completely normal sleep pattern, but about half showed 40 - 90 min cyclical periods of slow wave sleep that approached a normal sleep pattern.*

Conclusions: *Traditional classifications of EEG sleep staging are deficient when used to describe sleep in intensive care unit patients. (Critical Care and Resuscitation 2001; 3: 86-91)*

Key words: Sleep, bispectral index, electroencephalogram, intensive care

Lack of sleep in intensive care unit patients is thought to be a common problem. Many factors may contribute to this including the type and severity of the patient's illness, drugs used in the patient's management, and the ICU environment - which tends to be noisy, busy and associated with intensive monitoring.^{1,2}

Sleep deprivation can cause impaired patient cognition, which may result in apathy, confusion and delirium. It may also have an effect of impairing protein synthesis, cell division and cellular immunity, thus altering normal healing.³ Together these effects may cause an increase in morbidity and mortality.⁴

Although it is widely held that insomnia is common in intensive care unit (ICU) patients, we were only able to find data on proper electroencephalograph (EEG) quantification of sleep patterns in a total of 27 ICU patients from two studies.^{5,6}

Conventional EEG recording divides normal sleep into rapid eye movement (REM) sleep and non-REM

sleep. Non-REM sleep is subdivided into four further stages. Stage 1 has low amplitude, high frequency waves and is a state of light drowsiness. Stage 2 is the first unequivocal stage of sleep and is associated with short bursts of α -like activity on the EEG, known as 'sleep spindles' and 'K complexes'. Stages 1 and 2 are also called light sleep. Stages 3 and 4 are characterised by the emergence of larger waves of lower frequency and are known as 'slow wave sleep' (SWS) or deep sleep. In a normal individual, stage 1 is usually short, lasting 10 - 20 minutes, or 2 - 5% of the total sleep time (TST). Stage 2 initially lasts about 15 minutes and is followed by a period of SWS. Slow wave sleep generally comprises of 13 - 23% of TST, mainly in the first third of the night.^{7,8} REM sleep is usually observed first, about 70 - 90 minutes after the onset of sleep. REM periods (20 - 25% of TST) then cycle approximately every 90 minutes, alternating with stage 2 (45 - 55% of TST) and SWS, gradually increasing in length and intensity as the night progresses. Most young adults

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sleep approximately 7 ½ - 8 hours a night and most are able to maintain daytime alertness, provided their TST is > 5 hours.

Because of the difficulties of carrying out full EEG polysomnography in the ICU environment, we used the Bispectral Index (BIS) as an indicator of sleep patterns. There have been several studies describing the effects of sedation on the BIS,⁹ and one study that has shown a good correlation between the BIS and the level of natural sleep.¹⁰ Furthermore, from our unpublished data of ten healthy adult volunteers, we have seen cyclical changes in BIS values that were in phase with sleep stage changes as determined by a simultaneous full EEG recording.

An example of a typical pattern of the obvious changes in the BIS, during a night of normal sleep in a healthy volunteer, is shown in figure 1. The relatively good correlations between conventional sleep stages (as described above) and the BIS can be seen.

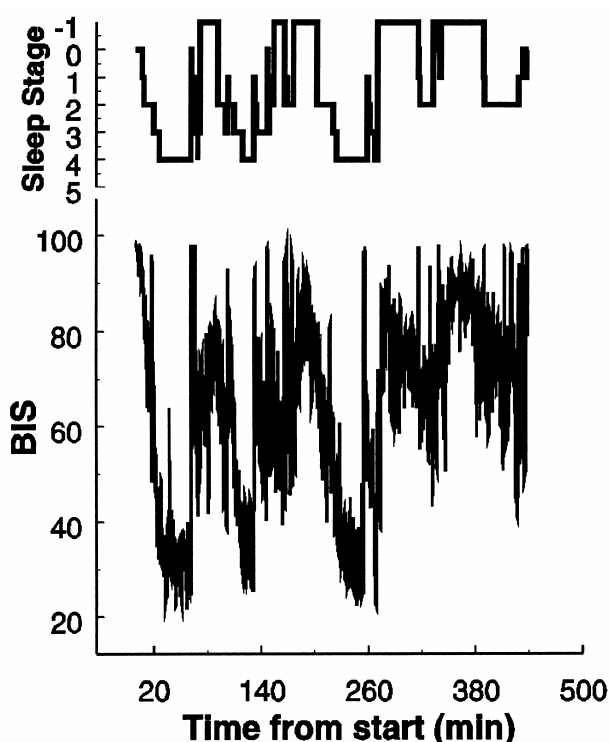


Figure 1. Plots showing normal alterations in sleep stage and Bispectral Index in a sleeping volunteer throughout the night (- 1 = REM sleep, 0 = awake, 1 and 2 = light sleep, 3 and 4 = slow wave sleep)

The aim of this present study was to use the BIS to quantify the sleep patterns found in adult patients in the ICU, and to attempt to identify any particular clinical factors that may contribute to the occurrence of normal, or abnormal sleep.

MATERIALS AND METHODS

Patients

After regional ethical committee approval, twenty-nine adult patients were studied in the ICU at Waikato Hospital between December 1998 and December 1999. Consent for the study was obtained for all participants, either directly or from the next of kin. Those who were chosen were considered to be in the recovery stage of their illness, and were either on small, decreasing doses of sedation, or had been weaned off sedation altogether. Patients who had been on psychotropic medication prior to their acute illness were not included. Two of the patients withdrew after a short time of monitoring, and were not included in the final analysis of the data. Of the remaining 27, there were 17 males and 10 females, with an overall mean age of 64 years (range 15 - 82 years).

For each patient we recorded the type (9 medical and 18 surgical), and duration of stay in ICU (mean 5.3, range 1 - 23 days). We also noted the patient's respiratory status (mechanically ventilated or not), renal function (plasma creatinine level), type, dose and duration of sedation during the ICU stay prior to the study night, and inotropic support (noradrenaline, adrenaline or dopamine infusion). In addition, we recorded their daytime alertness (alert and spontaneous, responding to voice, responding to pain and not responding). Those patients who had previously received a large dose of morphine (≥ 100 mg total dose) were grouped together and compared with a group who had received < 100 mg morphine. Similarly, those who had received a large dose of midazolam (≥ 100 mg total dose) compared with a group who had received < 100 mg of midazolam. The occurrence of these factors were then correlated with the patient's sleep pattern.

Data collection and analysis

An Aspect A-1000 (Aspect Medical Systems, Natick, MA, software version 3.12) EEG monitor was used. Three silver silver-chloride EEG electrodes (Ziprep, Aspect Medical Systems, USA) were attached to the patient's forehead after cleaning the skin with alcohol. One was used as the 'ground' (Fpz) and the other two were placed over the left and right prefrontal cortex (F7 - F8) to give a bifrontal bipolar signal. The high-pass and low-pass filters were set to 0.25 Hz and 50 Hz respectively. In addition, two electrodes were attached to the submental region to give an electromyographical (EMG) recording of facial muscle activity. From this channel we hoped to detect the hypotonia needed to distinguish between REM sleep and light sleep. The impedance of all electrodes was less than 20 k Ω . Visual inspection of the BIS waveform was made, and the processed data from the Aspect monitor

(BIS, 95% Spectral Edge Frequency and the spectral power in the alpha, beta, delta and theta wavebands) were downloaded onto the computer at 5 s intervals for subsequent analysis. Recordings were made overnight between 10 p.m. and 8 a.m. Clinical assessments of changes in the patient's level of consciousness were made during the recording of the BIS.

On the basis of the previous study, and in accordance with other unpublished observations from a pilot study of 10 normal volunteers, we made the following simplified classification of sleep stages:

- 1) BIS > 85 and clinically awake = AWAKE
- 2) BIS 60 - 85 = LIGHT SLEEP
- 3) BIS < 60 = SLOW WAVE SLEEP
- 4) REM Sleep. We used criteria for diagnosing epochs of REM sleep modified from Holzmann et al.¹¹ These are: i) A BIS value in the range of light sleep or awake (BIS > 60), and either ii) A decrease in EMG power > 30% or, iii) the presence of 'sawtooth' waves or rapid eye-movement artifacts on the (frontal) EEG waveform. The EMG power was estimated by using logarithm to the base10 of the 5 s median absolute deviation of the submental EMG signal. From our pilot study we estimated the accuracy of this classification to be around 80% correct (i.e. comparable with other automated somnogram systems).

Using the data stored on the computer we determined the durations of SWS, REM, and TST for each patient.

Classification of sleep patterns

We had hoped to classify the ICU patients into 'normal' and 'abnormal' according to the TST and percentage SWS and REM sleep. However, it became clear that the usual nomenclature of describing the sleep patterns was inadequate to describe the bizarre changes in EEG activity found in most ICU patients. None could be said to have a completely normal sleep pattern as is found in healthy subjects. We therefore grouped the patients into:

- 1) NIL = those who had no sleep at all,
- 2) CYCLICAL = those who had slow (40 - 90 min) cycles of alternating light sleep and SWS (this pattern was considered to be closest to normal sleep patterns), and
- 3) ABNORMAL = those patients with a variety of other atypical patterns. Most showed multiple brief 'naps' (i.e. periods of light or SWS of < 10 minutes duration). However, there was an extreme group in whom there were periods of very rapid transition to

low BIS levels (~60), and then up to ~95 again, failing to spend any significant length of time at the lower levels. We termed this a 'flickering' pattern. The three co-workers independently classified the patterns in a blinded fashion, and then compared their results – they were the same in all cases.

Statistical Analysis

Statistical analysis was performed using the NCSS statistical programme (NCSS 6.1, Kaysville, Utah). Correlations between EEG variables were calculated using Pearson's correlation coefficient (*r*). A *p* value of < 0.05 was considered significant. Fisher's exact test was used to quantify statistically significant associations between patient variables and the type of sleep pattern seen. Power calculations were performed using the Power Analysis Statistical System (PASS 1.0, NCSS, Kaysville, Utah).

RESULTS

Overall, there was a good correlation between the clinically observed level of consciousness and their BIS score. The mean sleep time was 98 min (42.4 minutes SWS, 3.7 minutes REM). Typical examples of the different sleep patterns are shown in figure 2. Twelve of the patients were classified as having a CYCLICAL sleep pattern (figure 2a), three had no sleep (figure 2b), and 12 showed ABNORMAL patterns (figure 2c), with a subset of three in this group showing an abnormal 'flickering' (figure 2d). Many of the ABNORMAL group at times appeared to be in a REM-like state – having a high BIS but, clinically, a low level of consciousness. An example of this is shown in figure 3. The patient's BIS abruptly flicked between 60 and 90 with no change in the clinical level of consciousness. This could not be attributed to shivering, because the EMG power did not change (EMG:BIS *r* = 0.11, NS). There were no detectable eye-movements, thus it could not fulfil even the most inclusive definitions of REM sleep. It was apparent that, in this state, the patient had periodic episodes of excessive high-frequency EEG spectral power causing fluctuations in the BIS. These were manifest in the frequency domain as changes in the BetaRatio, and in the bispectrum as concurrent changes in the Synch Fast Slow.

Both these indices are sub-parameters that contribute to the BIS.^{12,13} Both correlated significantly with the BIS (BIS: BetaRatio *r* = 0.43, *p* < 0.01; BIS: SynchFastSlow *r* = 0.47, *p* < 0.01), but not with the EMG power (BetaRatio:EMG *r* = 0.07, NS; SynchFastSlow:EMG *r* = 0.02, NS). This would tend to exclude high EMG artifact as a spurious cause for the high BIS values.

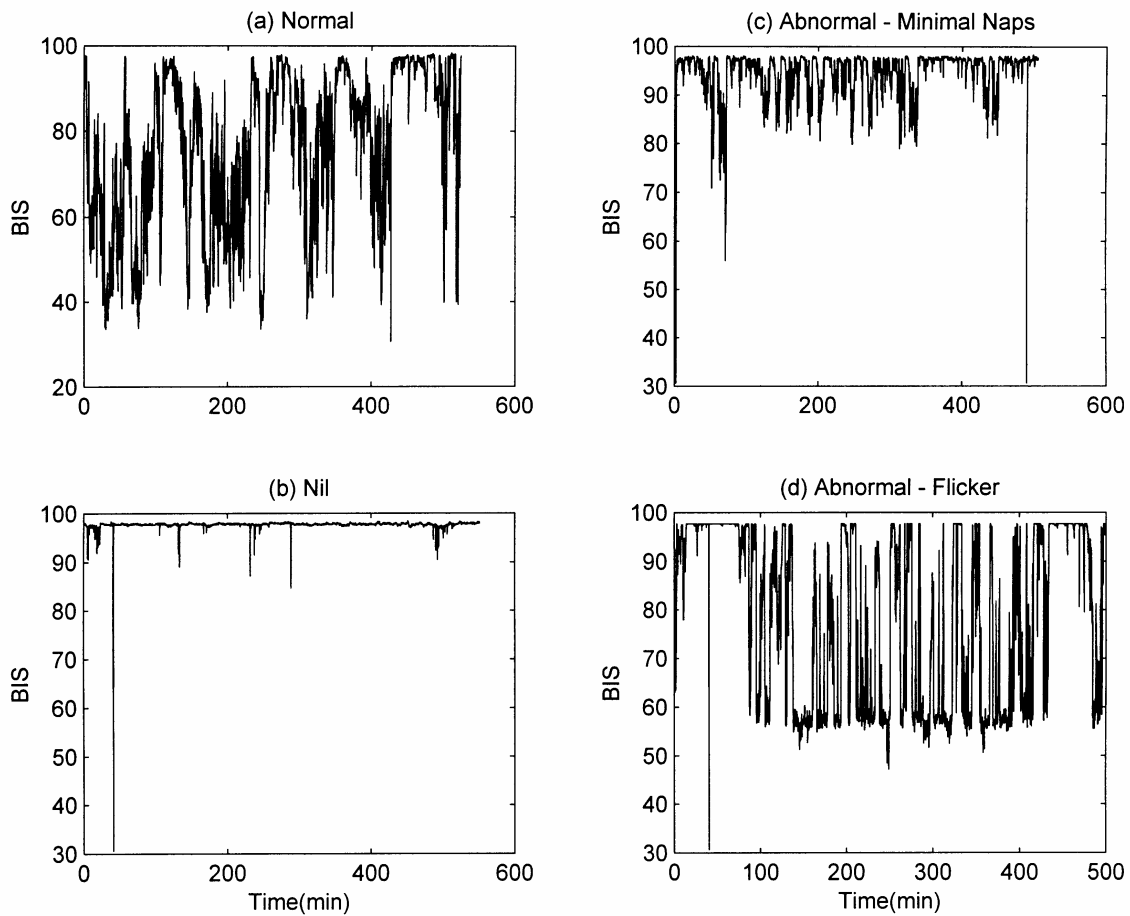


Figure 2. Examples of the 4 typical patterns of Bispectral Index found during the night in the intensive care patients. a) ‘normal’ cyclical pattern alternating between light sleep and slow wave sleep, b) ‘nil’ or no sleep, c) abnormal ‘minimal naps’ d) abnormal ‘flickering’ pattern

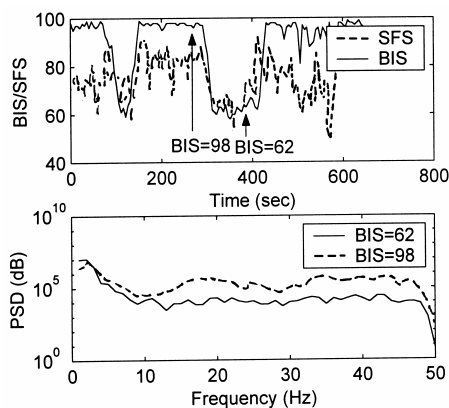


Figure 3. An enlarged segment of the bispectral index (BIS) trace in an ‘abnormal-flickering’ group patient. The upper graph shows the changes in the BIS, and concurrently, the changes in a subparameter of the BIS, SynchFastSlow (SFS). The lower graph compares two power-spectral density plots taken at the times shown in the upper graph: when the BIS was high (BIS = 98), and when the BIS was low (BIS=62), showing the increase in high-frequency (> 15Hz) EEG power that cause the high BIS values.

Thus although we were unable to detect the characteristic hypotonia and eye-movements of REM sleep, this state was probably akin to REM sleep, having unconsciousness coupled with a predominantly high frequency desynchronized (‘alert looking’) EEG pattern and a high BIS value.

We failed to find any statistically significant associations between the type of sleep pattern seen and the type and dose of sedation used, the type of illness, the length of time spent in ICU, the use of sympathomimetic agents, plasma creatinine and mechanical ventilation. This information is summarised in Table 1. Although it did not reach statistical significance, there was a tendency for proportionately more patients with impaired renal function (as estimated by plasma creatinine), or high-dose morphine to have abnormal sleep.

DISCUSSION

Using EEG techniques, we have objectively confirmed the clinical observation that almost no ICU patients

Table 1. Possible factors predictive of abnormal sleep patterns

Group	Number of patients with Zero or abnormal sleep	Number of patients with cyclical sleep	p value
Cumulative morphine dose \geq 100 mg	5	2	1.0
Cumulative morphine dose $<$ 100 mg	6	4	
Cumulative midazolam dose \geq 100 mg	6	3	1.0
Cumulative midazolam dose $<$ 100 mg	2	2	
Use of propofol	6	7	0.46
Use of morphine	11	6	
Sedation off $<$ 48 hr	4	6	0.19
Sedation off $>$ 48 hr	9	3	
No sedation used	3	1	0.60
Sedation used	12	11	
Surgical illness	9	9	0.68
Medical illness	6	3	
\leq 5 days in ICU	10	10	0.41
\geq 6 days in ICU	5	2	
No sympathomimetic agents used	7	4	0.69
Sympathomimetic agents used	8	8	
Plasma creatinine $<$ 0.2 mmol/L	8	11	0.20
Plasma creatinine \geq 0.2 mmol/L	6	2	
Not mechanically ventilated	7	4	0.74
Mechanically ventilated	9	8	

ICU = Intensive care unit, Sympathomimetic agents = adrenaline, noradrenaline, dobutamine or dopamine,

have normal sleep. This study also strongly highlighted the fact that the conventional criteria for sleep staging probably have a very limited application in describing the complex electrophysiological processes occurring in recovering ICU patients. Unfortunately the neurosciences have not progressed to the point whereby it is possible to confidently understand the significance of the underlying neurophysiological activity that cause the observed EEG patterns. Nevertheless, we are able to make some tentative statements. Firstly about half the patients have acceptable periods of SWS. Secondly, in ICU patients true REM sleep is rare. However "REM-like" states are quite common. There is a large body of evidence suggesting that exaggerated high-frequency (so-called 'gamma-band') EEG activity is caused by neuromodulator-induced (mainly cholinergic) depolarisation in the frontal cortex.^{14,15} Therefore, these states may be better termed 'hyper-cholinergic sleep/coma'. It is unknown if these REM-like states have any of the, functionally beneficial, restorative effects of true REM sleep.

In all cases, the patients had less sleep than would be expected for a normal person. The noisy ICU environment with its invasive and intensive monitoring is not conducive to sleep. As far as possible attempts are always made in the ICU to preserve a diurnal sleep/wake

rhythm, with the lights being dimmed at night and staff making an effort to be quiet. We chose to measure only nocturnal sleep patterns since we felt that these would demonstrate differences or similarities to the usual sleep pattern, which is primarily nocturnal, and because the nocturnal environment is more controlled in ICU than the daytime one.

Unexpectedly, the type, dose, duration, and time since stopping sedation, did not show any significant relationship to the sleep pattern. We had expected that those patients who had been on large doses of morphine for a long time, or those who had impaired renal function, or who had sedative agents stopped recently, would show an abnormal sleep pattern - due to the development of drug withdrawal. For example, Aurell and Elmqvist have showed morphine to have profound effects on sleep and to be associated with severe sleep disturbances.⁵ Krachman *et al* described a decrease in REM sleep and increase frequency of arousals and stage 1 sleep due to opioids.¹ Aurell and Elmqvist also believed that high doses of hypnotics may counteract the ability to sleep.⁵ However, in our study some of those patients who had received the largest doses of morphine, showed cyclical sleep activity, resembling a normal pattern. The three patients with the 'flickering' pattern had all received large doses of morphine.

Although a larger study may have detected small statistical correlations, we set out to detect only potentially clinically obvious effects, and calculated the power of our present study accordingly.

In conclusion, we found that no ICU patients showed a completely normal sleep pattern, but about half showed 40 - 90 minute cyclical periods of SWS that approached a normal sleep pattern. We failed to find any strong association between the sleep pattern and the dose, type or time from ceasing sedative agents, the time spent in ICU, use of inotropic agents, mechanical ventilation or plasma creatinine levels. Although true REM sleep seems to be rare in ICU patients, it is possible that abnormal REM-like states are not uncommon, and may conceivably fulfil similar physiological functions to true REM sleep. The degree to which conventional sleep nomenclature applies to ICU patients is a matter for further investigation.

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