# Bispectral Index Values and Spectral Edge Frequency at Different Stages of Physiologic Sleep

Diederik Nieuwenhuijs, MD*, Emma L. Coleman, BSc†, Neil J. Douglas, FRCP†, Gordon B. Drummond, FRCA‡, and Albert Dahan, MD, PhD*

*Department of Anesthesiology, Leiden University Medical Center, Leiden, The Netherlands; †Scottish National Sleep Laboratory; and ‡Department of Anaesthesia, Critical Care and Pain Medicine, Royal Infirmary, Edinburgh, United Kingdom

Bispectral index (BIS) and spectral edge frequency (SEF) are used as measures of depth of anesthesia and sedation. We tested whether these signals could predict physiologic sleep stages, by taking processed electroencephalogram measurements and recording full polysomnography through a night's sleep in 10 subjects being investigated for mild sleep apnea/hypopnea syndrome. Computerized polysomnograph signals were analyzed manually according to standard criteria, classifying each 30-s epoch as a specific sleep stage. The BIS and SEF values were taken at the end of each period of sleep when the same stage had lasted for at least 2 min. Before sleep, median values for BIS were 97 ± 12.1 and for SEF 23 ± 4.2 Hz. After sleep initiation, the median BIS values for arousal, light, slow wave, and rapid eye movement sleep were 67 ± 20.2, 50 ± 16.5, 42 ± 11.2, and 48 ± 7.1, respectively, and the median SEF values were 20 ± 4.7, 15 ± 3.6, 10 ± 2.6, and 19 ± 4.1 Hz, respectively. Although both BIS and SEF decreased with increasing sleep depth, the distribution of values at each sleep depth was considerable, with overlap between each sleep stage. Neither BIS nor SEF reliably indicated conventionally determined sleep stages. In addition, the response of the BIS was slow and patients could arouse with low BIS values, which then took some time to increase.

(Anesth Analg 2002;94:125–9)

Measures of awareness based on the electroencephalogram (EEG) often involve *ad hoc* processing to obtain an easily understood and rapidly available signal. A recent example is the bispectral index (BIS), which determines, among other things, the coherence between different frequency components of the frontal EEG waveform. The BIS correlates to wakefulness (1), learning (2), and the conscious processing of information (3). However, the device available for BIS measurement was designed and calibrated for use in anesthesia and is more commonly used to measure cerebral activity during anesthesia (4), and predict movement response to laryngeal mask insertion (5), intubation (6), and skin incision (7). Nonetheless, the BIS is not a specific index of consciousness (8). Despite this disadvantage, a recent study from Sleigh et al. (9) suggests that the BIS values correlate well with sleep stage. Because automatic measurement of sleep stage would be an asset in postoperative studies, we compared BIS and 95% spectral edge frequency (SEF), i.e., the frequency below which 95% of the power in the spectrum resides (10), with measures of sleep state obtained by standard polysomnography (11).

## Methods

We studied 10 patients (mean age 38 yr, range 25–54 yrs; 6 men, 4 women) suspected of having mild sleep apnea/hypopnea syndrome (SAHS). They were having routine polysomnographic investigation in the Scottish National Sleep Laboratory as part of their medical management. We consulted our local human ethics committee who agreed that written informed consent for measurement of additional processed EEG signals as well as the standard measurement devices was not necessary. We obtained consent from each patient for the additional recordings. We placed electrodes for the BIS (BisSensor; Aspect Medical Systems,

This study was supported by a grant for international collaboration from the Wellcome Trust and by the Netherlands Organization for Pure Research (NWO), The Hague, The Netherlands, Grant MW 902-21-211.

Accepted for publication August 28, 2001.

Address correspondence and reprint requests to Dr. D. Nieuwenhuijs, Department of Anesthesiology, Leiden University Medical Center (P5-Q) PO Box 9600, 2300 RC Leiden, The Netherlands. Address e-mail to djfn@worldonline.nl.


0003-2999/01

Newton, MA) on the head as specified by the manufacturer and measured signals with an Aspect A-2000 EEG monitor (software version 3.3; Aspect Medical Systems). For the polysomnograph, we placed two midline frontoparietal electrodes for EEG, electrodes at each canthus and above each eye for the electrooculogram, and two submental electrodes for the electromyogram. The subjects rested until 10:00 PM, when the lights were turned out and the recording started.

The polysomnograph variables were recorded with a computerized 16-channel recording system (Compumedics, Melbourne, Australia). The recorded signals from all of the subjects were analyzed manually by the same trained sleep technician according to standard criteria (11). Each recording was divided in epochs of 30 s and each epoch classified as one of the following sleep stages: awake (i.e., roused from sleep), stage 1, 2, 3, or 4 sleep, or rapid eye movement (REM) sleep. BIS in arbitrary values from 0 to 100, SEF (units Hz), and signal quality index (SQI) (percent satisfactory values) were recorded at 5-s intervals from the serial port of the A-2000 monitor to a laptop computer (Toshiba Satellite Pro 4200; Toshiba, Tokyo, Japan), by using the Microsoft HyperTerminal program (Hilgraeve, Monroe, MI). For further analysis, values of the BIS and SEF were obtained at the end of each period of uniform sleep/roused stage and note was taken of the duration of this period. Only stages lasting 2 min or more were included in the analysis (stable sleep/awake state). Signals with an SQI <50% were not analyzed.

The distribution of BIS and SEF values for each sleep stage was not normal. We used descriptive nonparametric statistics to examine the relationship between these signals and the categories of sleep. All values were presented as median (lower [25%] and upper [75%] interquartile values) and SD unless otherwise stated. To simplify the presentation of the data, and because relatively little time was spent in sleep stages 1 and 3, we considered stages 1 and 2 as "light sleep" and stages 3 and 4 as "slow wave sleep" (SWS).

## Results

All subjects completed the study. Four patients had more than 15 apneas or hypopneas per hour of sleep (apnea/hypopnea index). In the presence of symptoms (daytime tiredness), this meets the definition of SAHS (12). The mean apnea/hypopnea indexes for these subjects over the night were 27, 25, 27, and 19.

From polysomnography, the median recording time (i.e., time in bed) was 470 min (451–500 min); the median time subjects needed to fall asleep was 8 min (4–15 min); median sleeping time was 412 min (396–458 min); and median time aroused was 49 min (35–60 min). Of the time spent asleep, 11 min (8–12 min; 2.5% of total sleep time) was scored as stage 1, 253 min (220–267 min; 59.1% of total sleep time) as stage 2, 16 min (10–18 min; 3.5% of total sleep time) as stage 3, 60 min (48–78 min; 15.7% of total sleep time) as stage 4, and 80 min (53–98 min; 18.9% of total sleep time) as REM sleep. The sleep efficiency (time asleep/time in bed) was 89% (84%–91%).

From the BIS analysis, SQI was >50% during the studies in 9 subjects. In one subject, multiple episodes of SQI <50% were observed (45% of sleep time), and these data were not used. Before the subjects fell asleep, their median BIS values were 97 (94–98) ± 12.1 and their median SEF values were 23 Hz (20–25 Hz) ± 4.2. The BIS and SEF values both decreased with increasing sleep stages (Fig. 1), but the overlap in values at each stage was considerable (Figs. 2 and 3). After sleep initiation, the median BIS values for light sleep (stages 1 and 2 sleep) and SWS (stages 3 and 4 sleep) were 50 (44–65) ± 16.5 and 42 (35–49) ± 11.2, respectively, and the median SEF values were 15 Hz (13–18 Hz) ± 3.6 and 10 Hz (9–11 Hz) ± 2.6, respectively. During REM sleep, the respective BIS and SEF values were 48 (44–51) ± 7.1 and 19 Hz (16–21 Hz) ± 4.1. Arousal caused increases in BIS and SEF values to 67 (52–88) ± 20.2 and 20 Hz (15–22 Hz) ± 4.7, respectively. These BIS values (after arousal) were significantly different from presleep awake values (see above) ($P < 0.01$, $\chi^2$ test). SEF aroused and presleep awake values did not differ ($P = 0.06$).

## Discussion

We tested whether the BIS and SEF, two readily available processed EEG variables from the Aspect A-1000 and A-2000 monitors, were able to predict physiologic sleep stages reliably. For practical reasons, we took the opportunity to study patients who were being investigated for SAHS. Consequently, our subjects cannot be considered to be representative of the normal population, and four proved to have mild SAHS. Sleep architecture in these subjects was mildly disturbed, and normal in the others.

Our subjects were studied in the sleep laboratory and may not have slept as well as at home. However, we hoped to apply the BIS measurements in circumstances in the hospital where sleep quality is disturbed, such as after surgery and in high-dependency units, so this is not necessarily a weakness in this study. We selected sleep periods that had not been interrupted for at least two minutes (stable sleep), and sampled only the BIS and SEF signals from the end of the stable sleep stages. The BIS signal is derived from at least 15 seconds of preceding data [variable calculation, moving average, and artifact rejection (13)], so this precaution should provide values that would allow the BIS and sleep state values to agree. In practice,

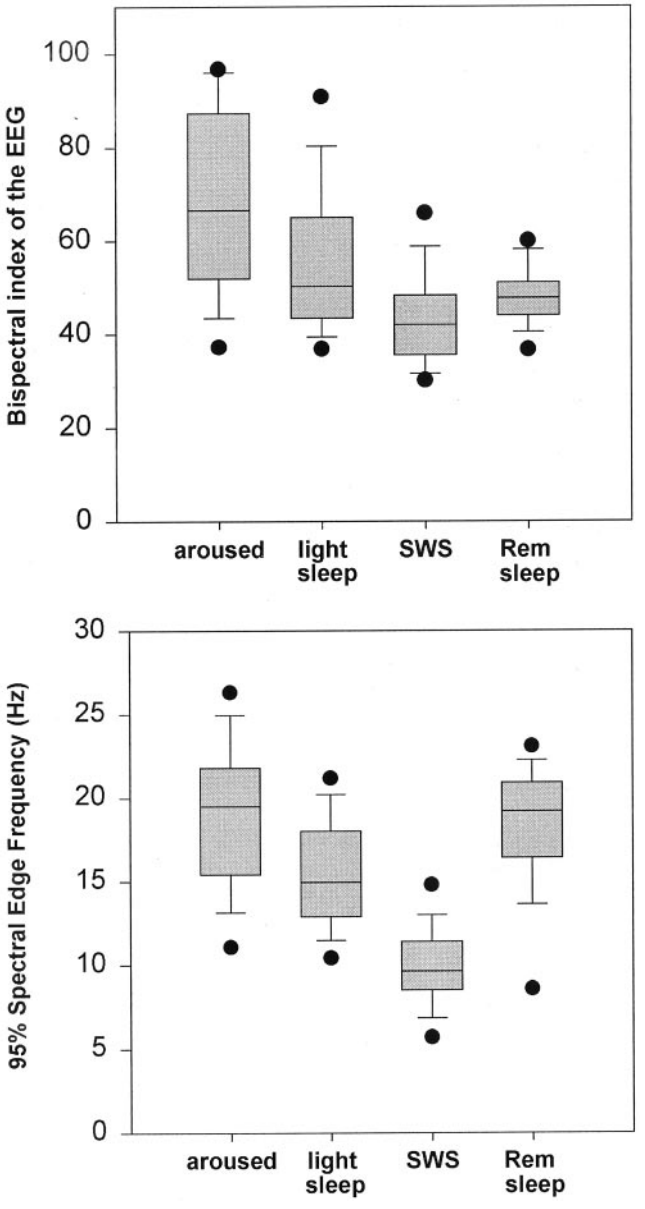


**Figure 1.** Box plots of the bispectral index of the electroencephalogram (EEG) (top) and 95% spectral edge frequency (bottom) values for each sleep stage (aroused, light sleep, slow wave sleep [SWS], and rapid eye movement [REM] sleep; presleep awake values not included). The heavy lines indicate the median, the boxes the quartiles, error bars the standard deviations, and the closed circles the range of the values.

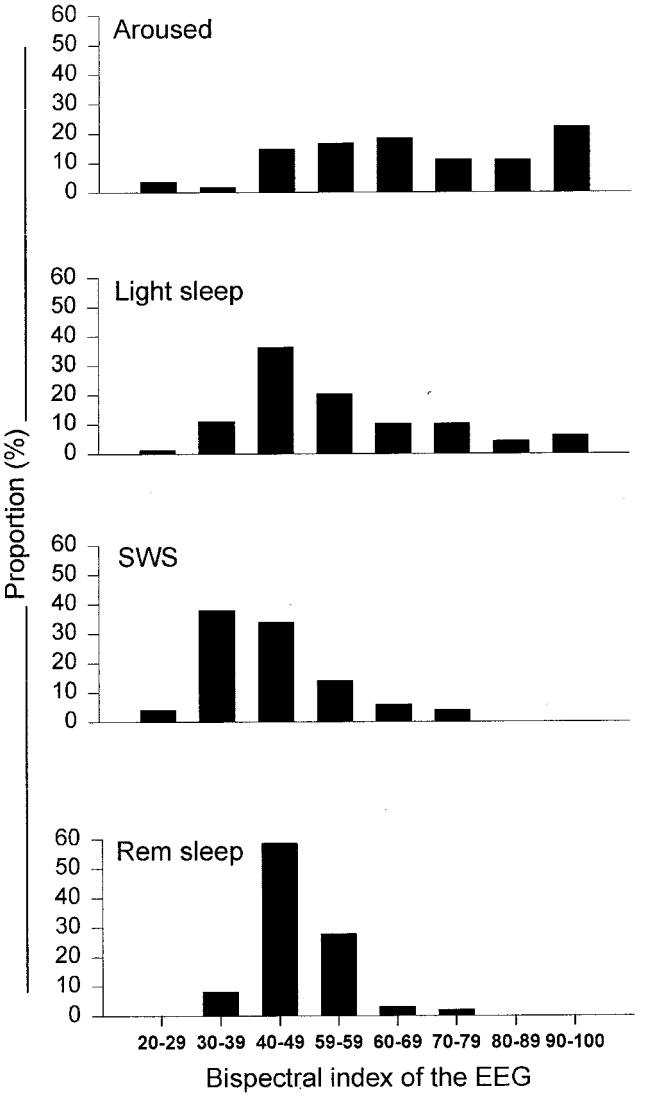


**Figure 2.** Distribution patterns of bispectral index values of the electroencephalogram (EEG) in aroused, light sleep, slow wave sleep (SWS), and rapid eye movement (REM) sleep (presleep awake values not included).

if BIS was to be used as an automatic index of sleep state, this "selection" of stable signals would not be possible, and any possible concordance with sleep stage could be reduced further.

The BIS is a complex variable that, among other things, reflects the coherence of different frequency components of the EEG. It uses a combination of analysis in time and frequency domains, and generates the index in relation to a database that has been obtained from patients during stable anesthesia of different depths (10). It is thus to be expected that different degrees of drug effect can be predicted from BIS analysis. The BIS signal seems to be a valid measure of anesthetic effect; for example, the dose of anesthetic needed to generate a given BIS value is related to the age of the subject, in the same way as anesthetic potency measured conventionally by minimum alveolar concentration value is related to age (14). Nevertheless, BIS values can vary considerably, for a given dose of anesthetic, or a given drug effect. For example, approximately 50% of the BIS values obtained when end-tidal sevoflurane is 2% overlap with the values present when end-tidal sevoflurane is 1% (14), and BIS values at different sedation scores in patients given sevoflurane can overlap completely (15). Although

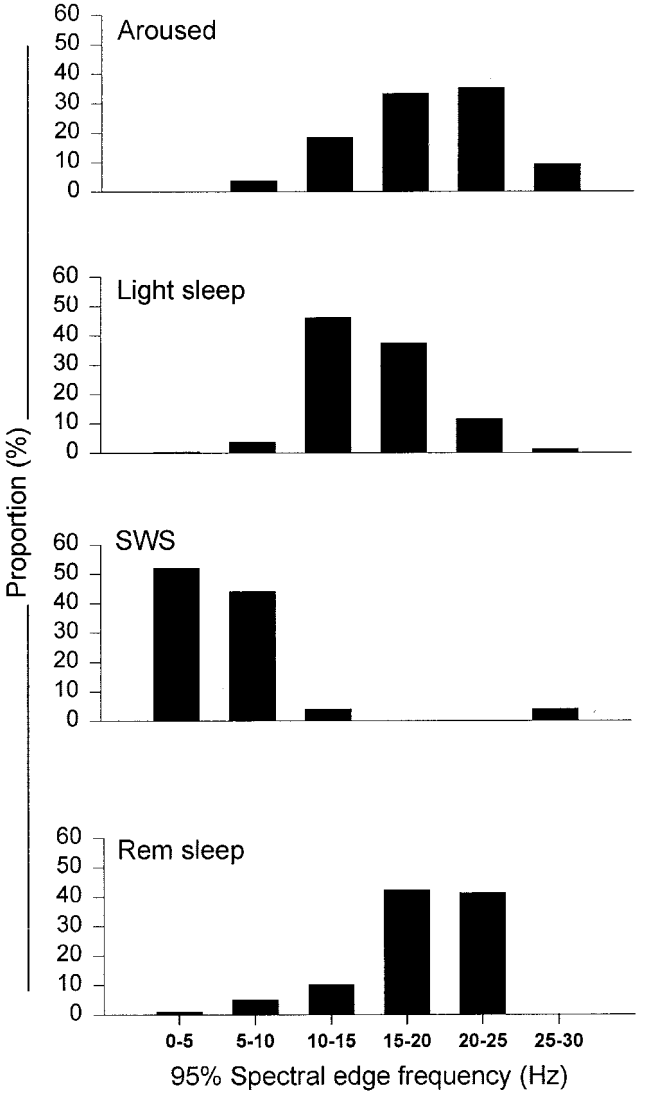


**Figure 3.** Distribution patterns of 95% spectral edge frequency values in aroused, light sleep, slow wave sleep (SWS), and rapid eye movement (REM) sleep (presleep awake values not included).

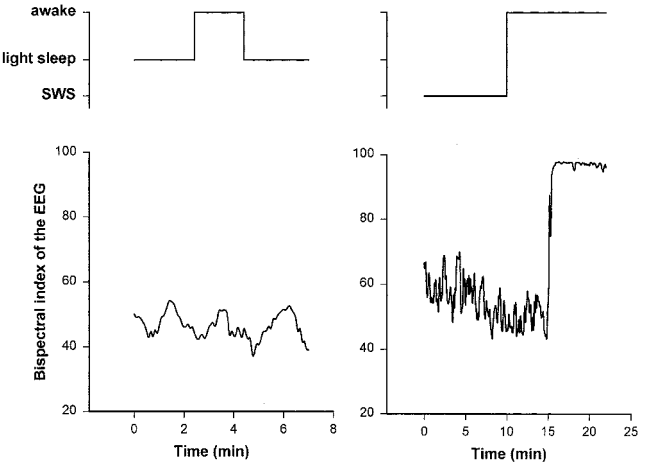


**Figure 4.** Examples of rapid arousals from light sleep (left) and slow wave sleep (SWS) (right). The bispectral index (BIS) values of the electroencephalogram (EEG) either did not change (left) or showed a delay of approximately 5 min before changing (right). The top panel represents the hypnogram of the polysomnography; the bottom panel represents the BIS values (values obtained at 5-s intervals).

others have suggested that values obtained by automatic processing of the EEG may indicate the depth of natural sleep, natural sleep is clearly not the condition that was used to "calibrate" the BIS device, and the capacity to predict sleep stage from BIS measurements has not been fully explored in previous reports (9). We explored this relationship in greater detail, because an automatic indicator of sleep state would be of great use in studies of postoperative breathing and respiratory control.

We observed a decrease in BIS values and SEF frequencies with increasing sleep depth from light sleep to SWS (Fig. 1). Although this suggests that both BIS and SEF are useful to discriminate sleep stages, the spread of values measured at each stage of sleep clearly precludes the use of these signals as measures of sleep stage. Fell et al. (16) used nonlinear methods to analyze the EEG during the different sleep stages. Their results indicate that nonlinear EEG measures (such as correlation dimension) yield additional information to the classical spectral measures in discriminating between sleep stages. However, the standard deviations of the measures at each of the sleep stages indicate considerable overlap for both spectral and nonlinear measures of the EEG, in agreement with our observations.

Our findings do not support those of Sleigh et al. (9). They measured BIS and SEF values in five volunteers who were sleeping at home. They reported greater BIS values for light sleep, SWS, and REM sleep than we did (light sleep 81 versus 50; SWS 59 versus 42; REM sleep 83 versus 48). However, they only analyzed the first sleep cycle of the night and restricted their analysis to testing for significant differences in the values measured at the start of each sleep stage, which may explain why the BIS values they report are considerably greater than those in the present study.

The BIS values we found in our aroused subjects were frequently lower than the values observed in the awake, presleep state. We suspect that this may be, in part, because the BIS value takes a long time to recover after arousal. Two examples of such a delay are shown in Figure 4. Because the BIS value output by the A-2000 represents the mean of at least 15 but sometimes 60 s of data (Olofsen and Dahan, unpublished observation), a delay of perhaps 1 minute might be expected, but in these examples, the delays are 2 minutes or longer. An alternative possibility is that the EEG and electromyogram features of arousal become apparent quickly, whereas the temporal synchrony measured by the BIS takes longer to dissipate after

arousal. During anesthetic measurements relating BIS to sevoflurane and isoflurane concentrations, the BIS seems to lag behind the calculated time for drug effect, and one potential explanation for this delay may be the slow changes in interactions between separate cortical regions (13).

Despite early results, it seems that processed EEG measurements (both BIS and SEF) have a limited ability to estimate classical sleep stages. Perhaps with a different "database" from naturally sleeping subjects, the BIS monitor could discriminate different physiologic as well as pharmacologic states.

The EEG monitor and electrodes were provided by Aspect Medical Systems International BV, Leiden, The Netherlands.

## References

1. Barnett TP, Johnson LC, Naitoh P, et al. Bispectrum analysis of electroencephalogram signals during waking and sleeping. Science 1971;172:401–2.
2. Leslie K, Sessler DI, Schroeder M, Walters K. Propofol blood concentration and the bispectral index predict suppression of learning during propofol/epidural anesthesia in volunteers. Anesth Analg 1995;81:1269–74.
3. Kearse LA, Rosow C, Zaslavsky A, et al. Bispectral analysis of the electroencephalogram predicts conscious processing of information during propofol sedation and hypnosis. Anesthesiology 1998;88:25–34.
4. Alkire MT. Quantitative EEG correlations with brain glucose metabolic rate during anesthesia in volunteers. Anesthesiology 1998;89:323–33.
5. Doi M, Gajraj RJ, Mantzaridis H, Kenny GNC. Prediction of movement at laryngeal mask airway insertion: comparison of auditory evoked potential index, bispectral index, spectral edge frequency, and median frequency. Br J Anaesth 1999;82:203–7.
6. Sleigh JW, Donovan J. Comparison of bispectral index, 95% spectral edge frequency and approximate entropy of the EEG, with changes in heart rate variability during induction of general anaesthesia. Br J Anaesth 1999;82:666–71.
7. Vernon JM, Lang E, Sebel PS, Manberg P. Prediction of movement using bispectral electroencephalographic analysis during propofol/alfentanil or isoflurane/alfentanil anesthesia. Anesth Analg 1995;80:780–5.
8. Gajraj RJ, Doi M, Mantzaridis H, Kenny GNC. Analysis of the EEG bispectrum, auditory evoked potentials and the EEG power spectrum during repeated transitions from consciousness to unconsciousness. Br J Anaesth 1998;80:46–52.
9. Sleigh JW, Andrzejowski J, Steyn-Ross A, Steyn-Ross M. The bispectral index: a measure of depth of sleep? Anesth Analg 1999;88:659–61.
10. Rampil IJ. A primer for EEG signal processing in anesthesia. Anesthesiology 1998;89:980–1002.
11. Rechtschaffen A, Kales A. A manual of standardized terminology, techniques, and scoring systems for sleep stages of human subjects. Bethesda, MD: National Institute of Health, 1968.
12. Cheshire K, Engleman HM, Deary IJ, et al. Factors impairing daytime performance in patients with sleep apnea/hypopnea syndrome. Arch Intern Med 1992;152:538–41.
13. Olofsen E, Dahan A. The dynamic relationship between end-tidal sevoflurane and isoflurane concentrations and bispectral index and spectral edge frequency of the electroencephalogram. Anesthesiology 1999;90:1345–53.
14. Denman WT, Swanson EL, Rosow D, et al. Pediatric evaluation of the bispectral index (BIS) monitor and correlation of BIS with end-tidal sevoflurane concentration in infants and children. Anesth Analg 2000;90:872–7.
15. Katoh T, Suzuki A, Ikeda K. Electroencephalographic derivatives as a tool for predicting the depth of sedation and anesthesia induced by sevoflurane. Anesthesiology 1998;88:642–50.
16. Fell J, Roschke J, Mann K, Schaffner C. Discrimination of sleep stages: a comparison between spectral and nonlinear EEG measures. Electroencephalogr Clin Neurophysiol 1996;98:401–10.