

EEG signal in monitoring brain function in anesthesia and intensive care: a review

Tarmo Lipping and Ville Jäntti

Tampere University of Technology, P.O. Box 300, 28101 Pori, Finland; tl@pori.tut.fi

Received 16 February 2004

Abstract. During recent years EEG has become the “golden standard” by estimating depth of anesthesia of individual patients in clinical work. Several monitors, based on processing EEG and showing graphically indices of “depth of anesthesia”, have been developed and millions of patients have been monitored with these. In this paper we first shortly discuss the terminology, particularly the meaning of “depth of anesthesia”. Next, a review of different methods and algorithms used in anesthesia monitoring is presented. Finally, we summarize the methods and outline the future development of anesthesia monitoring.

Key words: EEG, monitoring, anesthesia, sedation, hypnosis.

1. INTRODUCTION

The problem of consciousness is perhaps the biggest challenge of modern science. Anesthesiologists are privileged in studying it because they deliberately manipulate consciousness with different drugs in their daily work. The practical goal is to find methods for safe anesthesia without pain or recall for each individual patient.

Giving the right amount of drug for general anesthesia in operating room (OR) and sedation in intensive care unit (ICU) is important, because too light anesthesia results in recall of events and even pain in OR and too light sedation in a restless, anxious patient in ICU. Too deep anesthesia causes prolonged awakening times after operations and longer treatment times in ICU. The amount of hypnotic (sleep producing) and analgesic (pain killer) drugs needed to achieve appropriate anesthesia or sedation is mainly decided from experience with these drugs and clinical signs. Use of muscle relaxants can make the clinical evaluation impossible. This has led to the search for other, more “objective” measures to

optimize the level of sedation in ICU for the best treatment results as well as the depth of anesthesia in OR for the safety of patients and short recovery times.

Brain is the target organ of hypnotic drugs. It is therefore no wonder that soon after discovering human EEG, Berger started to study the effect of anesthetic agents on it. Already in the 1950s attempts were made to deliver anesthetic agents with a closed-loop control system, based on EEG quantification. After that, several brain function monitors were designed mainly for the ICU, but they were applied also in OR.

With the advancements of digital technology, the area of monitoring brain function and depth of anesthesia experienced a renaissance. Due to its flexibility, digital technology allows to apply a broad range of analysis methods to the signal and to monitor the results in the manner, most convenient for the medical staff involved. In this paper we give an overview of the developed methods starting with the historical Cerebral Function Monitor and ending with recently developed algorithms like Narcotrend and Entropy. This overview is by no means exhaustive. Our goal has been to concentrate on methods involving novel signal analysis at the time of their introduction. An important landmark in anesthesia monitoring is the development of Bispectral Index Score (BIS) by Aspect Medical Systems Inc. It is mostly due to the popularity of this method that using EEG signal in anesthesia monitoring has become standard practice in many operating rooms. BIS has also activated the development of new alternative methods and has since its introduction been the golden standard, against which new methods are tested. Even EEG controlled delivery of anesthetic drugs has become a subject of research again; however, at present the aim of these studies is better understanding and modelling of drug effects, not the development of a closed loop clinical anesthesia system.

2. EEG: THE ORIGIN AND MEASUREMENT

Spontaneous EEG is generated by the cerebral cortex. Pyramidal cells with cell nuclei, located in the 5th neuronal layer of the cortex, are considered to contribute most to the signal measured at the scalp. These neurons have dendrites, stretching perpendicularly to the scalp through neuronal layers 2–4 with synapses attached to them. The activation of the synapses causes current loops in the direction of the dendrites, and current flowing towards (away from) an EEG electrode in the medium outside the cells causes upward (downward) potential in it. For the activity to be detectable, large populations of pyramidal neurons have to be activated synchronously. Smaller areas of the cortex and subcortical structures produce potentials, which can be recorded with special techniques, such as signal averaging, when studying evoked potentials. Subcortical areas can also affect spontaneous EEG indirectly by causing the activation of the cortex. The changes in the EEG signal and specific patterns, seen in anesthesia and natural sleep, are mostly of this type of origin.

The EEG signal is most commonly recorded using the standard 10-20 system of electrode placement [1]. However, in the case of monitoring in OR, often only one or two electrodes, located at the forehead, are used to make the recording procedure simpler. The potential at the electrodes is filtered, amplified by analogue preamplifiers and then digitized. Usually frequencies below 0.5 Hz are removed in order to prevent the amplifiers from saturation due to drift in signal baseline. Also, frequencies above half the sampling frequency are removed to prevent aliasing. Sampling frequency varies a lot among different systems. Common wisdom is that spontaneous EEG does not contain frequencies above about 40 Hz, and 70 Hz is the traditional upper limit in routine EEG recordings. However, in some systems sampling frequencies above 1 kHz are used either to extract electromyographic (EMG) activity or enable monitoring of evoked potentials. In the SNAP monitor, frequencies up to 420 Hz are included in the analysis of spontaneous EEG. Interpretation of these results remains a subject of debate.

The frequency range of the recorded EEG signal is an important issue as the appearance of the waveform is highly dependent on the cutoff of the high-pass filter. In addition, research results indicate that very low frequencies of the EEG contain valuable information [2-4]. In modern EEG devices the signal is recorded with as broad frequency band as possible and the neurophysiologist can choose suitable digital filters later on while exploring the recording. However, in the case of monitoring the filters must be applied on-line.

The EEG signal is most often described by means of standard frequency bands: delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (12-20 Hz) and gamma (above 20 Hz). The exact frequency ranges may vary slightly in different sources.

3. EEG AND ANESTHESIA

When the patient is given increasing doses of anesthetics either in inhaled air, i.e., volatile anesthetics and nitrous oxide, or intravenously such as barbiturates and propofol, the EEG changes in a characteristic manner, roughly similar for most agents. First, 12-18 Hz activity appears, which turns into intermittent slow delta activity and widespread 8-14 Hz activity. After that, the relative amount of slow activity increases until short flat segments of EEG, called suppression, appear. Gradually suppression increases in duration, and the high amplitude segments, called bursts, shorten to produce a burst suppression pattern. Finally, the bursts disappear and the EEG is continuously in suppression.

3.1. Depth of anesthesia, depth of hypnosis and depth of sedation

Although depth of anesthesia is a useful term in OR, it is very difficult to define. For decades anesthesiologists believed that some day a common mechanism of producing unconsciousness would be found for all anesthetic drugs. This proved not to be true and Kissin in his classical paper concluded that the term "depth of anesthesia" actually vanishes [5]. The different mode of action

of different anesthetics becomes increasingly apparent with higher concentrations. In particular, the burst suppression pattern is very different with different drugs. Similarly, evoked responses such as somatosensory evoked potentials are very drug-dependent at deep levels.

During recent years “depth of anesthesia” has been often divided into “depth of hypnosis”, analgesia and relaxation. Depth of hypnosis, however, is equally impossible to define as depth of anesthesia due to different modes of action of different drugs.

In ICU small doses of anesthetics are given to make the patient calm, and this effect is called sedation. However, some drugs can only produce sedation but not surgical anesthesia. Anesthesia and sedation can be produced by different structures in the brainstem. The specificity of action appears at the level of cell membrane receptors: some receptors are responsible for sedation while others for general anesthesia.

Keeping these restrictions in mind, practice has shown that by using “depth of anesthesia monitors” excessively deep anesthesia, where EEG is in continuous suppression, can be avoided in some patients. The monitors probably can also warn about too light anesthesia, although statistically meaningful proof of this can be achieved only by collecting material from thousands of patients, as the occurrence of awareness during anesthesia is very rare. Numerous studies have shown that using these monitors makes the emergence from anesthesia faster, decreases the amount of anesthetic agent needed and allows the patient to be discharged from the OR more quickly. This is achieved without any increase in unwanted intraoperative events (movement, eye opening, grimacing, etc.).

4. OVERVIEW OF METHODS USED IN “DEPTH-OF-ANESTHESIA” MONITORS

4.1. Cerebral Function (Analyzing) Monitor (CFM, CFAM1-CFAM4)

The CFM family of brain monitoring devices has certainly the longest history. The first member of this family, the CFM, was developed in 1969 by D. Maynard at The London Hospital in Whitechapel [6]. This device was based on analogue technique and incorporated the following steps of analysis: band-pass filter (2–15 Hz) with amplitude compensation, logarithmic amplitude compression, and peak-to-peak rectifier. The result was written to a slow-speed chart recorder and consisted of two traces – one indicating the electrode impedance and the other the overall amplitude of the analysed EEG. This simple output was useful in the detection of suppression in ICU and operating theatre as well as in epilepsy monitoring.

The next member of the family, the CFAM1, was developed in 1975 by the same group [7]. This device already involved digital processing using Motorola 6808 8-bit microprocessor. The output trace is shown in Fig. 1. The upper plot shows the 10th centile, the mean and the 90th centile of the amplitude distribution

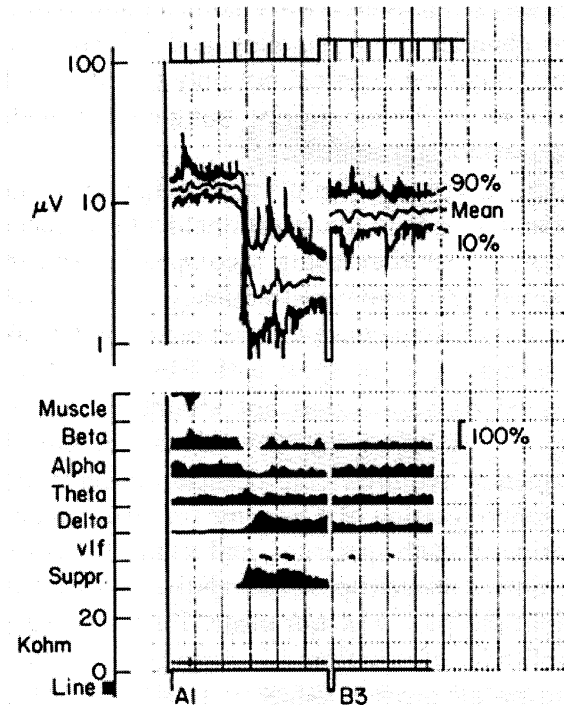


Fig. 1. Trace of the CFAM1 device (from Dr. Douglas Maynard with permission).

while the lower plot shows the percentage of weighted EEG activity per Hz in the beta, alpha, theta and delta frequency bands. In addition, the muscle activity, the percentage of recording time of the EEG suppression and the electrode impedance were monitored. Another advancement of the CFAM1 was the possibility of monitoring averaged evoked potentials.

The next version, the CFAM2 was first manufactured in 1989 by RDM Consultants. This was a two-channel device operating on a DOS-based system. A digital signal processor was used for signal filtering and FFT calculation. The monitored parameters remained principally the same as in CFAM1. However, the device enabled off-line reviewing and statistical analysis of the stored data. Also, manual categorization of the recording was possible and attempts were made for automatic classification. The software could be run on a standard PC as well. In the CFAM3, first manufactured in 1995, the software for automatic data classification could be run either on-line or off-line. The software for statistical analysis was developed further together with enhanced graphical displaying capabilities. The device could record and monitor 4 channels of EEG. The recently introduced CFAM4 is a cheaper and more compact version of CFAM3. Additional information about the CFM family of brain monitors can be found in [8].

4.2. Anesthesia Brain Monitor (ABM)

Datex-Ohmeda (Helsinki, Finland) introduced its first EEG monitor for anesthesia, the Datex Anesthesia and Brain Monitor, in 1982. The original version of the monitor was a one channel device while ABM2 used two channels, offering additional information about EEG symmetry. The electrodes were placed on the forehead. A special feature of this monitor was deriving EMG and EEG from the same signal using different filters (65–300 Hz for EMG and 1.5–25 Hz for EEG). EMG is valuable in detecting artifacts as well as the patient's response to stimuli during anesthesia. Only amplitude information (the root mean squared value) was calculated from EMG while amplitude together with the zero crossing frequency was monitored from EEG. The amplitude values were presented in logarithmic scale except in ABM2, where the EEG amplitude was presented in linear scale. The signal was analysed in 10 s consecutive windows. The ABM monitor is described in [9].

4.3. Advanced Depth of Anesthesia Monitor (ADAM)

At the beginning of 1990s, a different approach to anesthesia monitoring was taken by Thomsen et al. when developing the ADAM system [10,11]. They divided the signal into consecutive 2 s segments, applied a prewhitening filter, and derived 11 parameters: the RMS value and 10 coefficients of the autoregressive model (alternatively, correlation coefficients were used) from each segment. To create a set of reference classes, an unsupervised repetitive hierarchical cluster analysis was applied to the data bank of pre-annotated recordings. Subsequently, the clusters were mapped to a scale of six levels: from drowsiness to very deep anesthesia. The data bank contained recordings of halothane and isoflurane anesthesia and the classification was adjusted according to the agent used. EEG suppression was detected separately and the information about the ratio of suppression in 2 s segments was incorporated into the classification system. The classification results were summed over 10 s periods and monitored as a class probability histogram together with compressed spectral array and other physiological variables (Fig. 2).

In [12] the ability of four methods: median frequency, spectral edge frequency, the CFAM1 and ADAM to assess the anesthetic depth was compared. It was found that ADAM was the most invariant to the inter-patient variability due to its pattern recognition approach. However, this comparison is not totally fair as the first two are just single parameters and the CFAM1 was not developed primarily for anesthesia monitoring. Although ADAM was a very advanced system it was never used in a commercial monitoring device. One drawback of the system might be that the proposed monitor layout contained too much information and was thus too complex to be interpreted in a complicated clinical situation.



Fig. 2. Layout of the ADAM monitor; the second window from the left presents compressed spectral array, the class probability histogram is presented in the fifth window from the left (from Prof. Carsten Eckhart Thomsen with permission).

4.4. Bispectral Index Score (BIS)

The BIS, introduced by Aspect Medical Systems Inc. in 1997, certainly answered the need for a simple index measuring anesthetic depth. Its output is a single number between 0 and 100 achieved by combining in a non-linear fashion the following parameters [13]:

- relative beta ratio calculated in spectral domain as $\log(P_{30-47}/P_{11-20})$, where P_{30-47} and P_{11-20} denote signal power in frequency ranges 30–47 Hz and 11–20 Hz, respectively;
- SynchFastSlow measure calculated in bispectral domain as $\log(B_{0.5-47.0}/B_{40.0-47.0})$, where $B_{0.5-47.0}$ and $B_{40.0-47.0}$ denote the sum of magnitudes of the bispectrum values in the corresponding frequency ranges;
- burst-suppression ratio.

The weighting of the parameters depends on signal properties; however, the algorithm according to which the parameters are mixed is still not disclosed. The development of BIS was based on an extensive data bank of recordings of carefully controlled anesthesia and the parameters of the algorithm, including the mixing function, have been fine-tuned empirically. A very important, although sometimes overlooked part of the BIS algorithm, is the careful artifact rejection procedure preceding the analysis. The procedure incorporates several stages dealing with heartbeat artifacts, eyeblinks, wandering baseline and artifacts of high variance (like muscle artifacts, e.g.). An example of the dynamics of the BIS value in the course of a typical surgery is presented in Fig. 3.

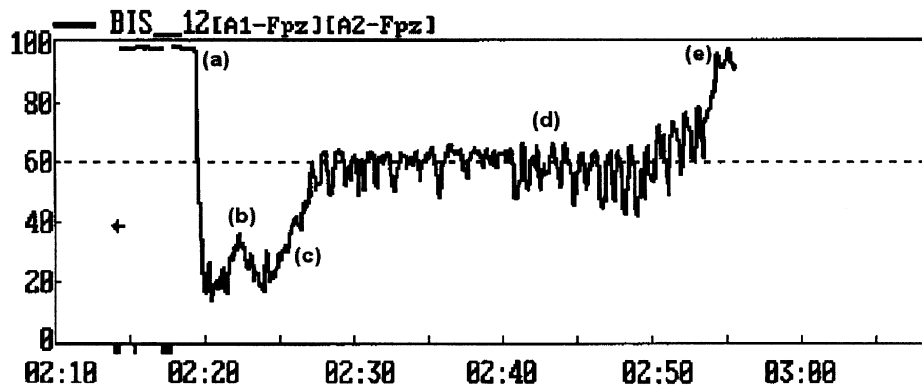


Fig. 3. An example of the behaviour of the BIS curve during surgical anesthesia: (a) beginning of anesthesia, (b) surgery, (c) lightening of anesthesia, (d) end of surgery, (e) the patient opens her eyes (from Prof. Arvi Yli-Hankala with permission).

Since its introduction, BIS has become very popular among anesthesiologists. It has caused a boom of papers, both in support of as against it. It has been found that BIS fails in several situations, e.g., when nitrous oxide or ketamin is used [14,15] and in the case of halothane anesthesia in children [16]. Also, frontal EMG activity, superimposed on the EEG, may lead to too high BIS values, especially during emergence from anesthesia. There has been discussion on whether bispectral analysis adds any real information to the BIS index and whether higher order spectral measures of the EEG (i.e., non-linearity of the signal) correlate with the level of consciousness [17].

4.5. Narcotrend

The Narcotrend[®] anesthesia monitoring system (MonitorTechnik, Bad Bramstedt, Germany) has its roots in sleep analysis. The five-stage (stages A–E) sleep analysis system, originally presented in [18], was further developed by Schultz et al. into a system of six stages and 14 substages (A, B₀₋₂, C₀₋₂, D₀₋₂, E₀₋₁, F₀₋₁), aimed at monitoring the level of hypnosis during anesthesia [19]. These scales have later on been mapped into the range 0–100 to be plotted in the form of a cerebrogram. The Narcotrend analysis system handles the EEG signal in 20 s segments [20]. The segments are overlapped so that a new value is obtained every 5 s. After artifact detection a set of parameters are calculated for each segment. The final list of parameters is not made public, however, the set is divided into time domain and frequency domain parameters. Time domain parameters include coefficients of the autoregressive model and in the frequency domain the division of the signal into standard EEG frequency bands is used. Also, spectral entropy is included in the parameter set. The parameters are classified using multivariate classification functions developed using multivariate discriminant analysis on manually classified test data. Burst-suppression, indicated by scale F, is detected

separately. Finally, plausibility check is performed to ensure that the segment is actually similar to a typical EEG sample of corresponding stage and to detect untypical patterns for general anesthesia (epileptic activity, for example).

Narcotrend Index like BIS has been shown to outperform single spectral parameters in indicating the level of hypnosis during propofol-remifentanyl anesthesia [21]. Also, Narcotrend monitoring allows faster emergence from anesthesia and reduced drug consumption compared to standard practice [20].

4.6. Patient State Index (PSI)

The PSI was developed a few years ago to be used in the PSA 4000 (Physio-metrix, Inc., N. Billerica, MA) anesthesia monitoring device. The algorithm behind PSI is described in [22]; however, the details are not disclosed. The algorithm yields a single number between 0 and 100 with smaller values indicating higher level of hypnosis. The development of PSI is based on three databanks: EEG library of 20 000 cases, a library of surgical procedures, and a library for calibration obtained from volunteer studies. Exploiting these extensive databanks enables the algorithm to take into account individual variability of the brain's response to anesthetic agents. Another important feature of PSI is that it is based on four fixed EEG channels: Fp1, Fpz, Cz and Pz with ground at Fp2 and reference at linked ear electrodes. Several features, extracted from the EEG signal and fed to the discriminant algorithm, include information about the relative power changes at different locations in certain frequency bands. For example, absolute power gradient between frontopolar and vertex regions in gamma frequency band is calculated. The full list of parameters as well as the discriminant algorithm is not made public. In the development phase, features based on the bispectrum and coherence have been used; however, whether these parameters were found to be among the ones correlating significantly with the level of hypnosis, is not disclosed. The PSI algorithm also includes careful artifact rejection and suppression detection.

In [22] it was found that using the PSI, the emergence time from anesthesia, verbal response time, extubation time and eligibility for operating room discharge time, all were shorter compared to control anesthesia cases not monitored with PSI. Also, comparison with BIS monitoring (results for BIS were obtained from [23]) showed that BIS and PSI give similar end points for emergence from anesthesia.

4.7. SNAP

SNAP is a device which in many ways breaks the rules of anesthesia monitoring. It was introduced by Nicolet Biomedical (Madison, WI, USA) in 2002. SNAP is meant to extend a Handspring Visor handheld PDA into an anesthesia monitor so that the anesthesiologist can keep track of his/her patient's level of anesthesia and organize the daily activities using the same convenient device. In addition to the appearance, the method for the assessment of the level

of anesthesia is uncommon either [24]. The EEG signal, obtained from Fp1-A1, is divided into two frequency bands: 0.1–20 and 80–420 Hz. From each band corresponding index is calculated by weighing spectral components of the signal. The high frequency index is scaled between 0 and 1 while the low frequency index is scaled between 0 and 100. The final index, the Derived EEG Index, is the product of the two scaled indices and is therefore a single number in the range of 0–100. The detailed description of the algorithm has not been published, the algorithm is fully based on spectral parameters and the analysis is performed using FFT. High frequency index forms a kind of scaling for the low frequency index. The output value is updated every 2 s and calculated over a window of 15 s.

In [24] a feasibility study of SNAP, incorporating data from 41 patients, has been presented. It has been reported that the algorithm performs in an expected way, indicating the level of anesthesia. Disturbance, caused by the electrosurgical unit, has been noted. Perhaps the main problem concerning SNAP is the interpretation of the high frequency EEG. Although in conventional analysis frequencies above about 40 Hz are discarded, evoked potentials (EPs), for example, contain components well beyond 100 Hz. However, these components are usually hidden in noise and in case of EPs they can be revealed by averaging hundreds of synchronized responses. Only extensive research can show if the components used in SNAP rise from noise (muscle activity, e.g.) or if they can be considered true EEG activity.

4.8. Entropy

Estimation of entropy, used in the Datex-Ohmeda Entropy™ Module (Datex-Ohmeda Division, Instrumentarium Corp., Helsinki, Finland), is based on the intuitive idea that the regularity of the EEG signal increases with deepening hypnosis and this can be quantified as signal entropy. There are various ways of quantifying entropy. In the Entropy™ Module, spectral entropy is used due to the relative simplicity of calculation as well as the possibility of obtaining the entropy value separately for specified frequency bands [25]. Compared to several other parameters used for anesthesia monitoring, entropy has the advantage of being independent of absolute amplitude and frequency of the signal, eliminating the need to count for interindividual variations. Normalized spectral entropy in the frequency range $[f_1, f_2]$ is calculated as

$$S_N[f_1, f_2] = \frac{S[f_1, f_2]}{\log(N[f_1, f_2])},$$

where

$$S[f_1, f_2] = \sum_{f_i=f_1}^{f_2} P_n(f_i) \log\left(\frac{1}{P_n(f_i)}\right).$$

Here $P_n(f)$ is the power spectrum normalized so that the sum of all the frequency components equals to 1 and $N[f_1, f_2]$ is the number of frequency values in the range $[f_1, f_2]$. It must be emphasized that this is not a measure of regularity or predictability but rather a measure of closeness to sinusoidal shape. A regular square wave, for instance, which is equally predictable as the sine wave, actually receives a spectral entropy value far higher than that of the sine wave.

The entropy module derives the EEG signal from a single frontal channel. In this derivation the muscle activity dominates over the EEG signal at frequencies above about 30 Hz. However, instead of discarding these high frequencies, the entropy monitor uses them to detect the early response of the patient to nociceptive stimuli. This is achieved by calculating separate entropy values for frequencies 0.8–32 Hz (state entropy), and 0.8–47 Hz (response entropy). The difference between these parameters shows the contribution of the EMG component to the response entropy.

There are several important details concerning the entropy algorithm. The signal is analysed in segments of different length depending on the frequency. The shortest time window used for analysing the frequencies between 32 and 47 Hz is 1.92 s while the longest one is 60.16 s. This property of the algorithm ensures that the patient's responses to nociceptive stimuli are detected as early as possible. The normalization of the entropy parameters is done so that the state entropy always corresponds to the part of the response entropy below 32 Hz. Thus the maximum value of the state entropy always remains below 1. This makes the parameters more informative for the anesthesiologist. Burst-suppression is detected using the algorithm presented in [26]. The entropy of suppressed EEG is considered to be zero while that of bursts is calculated as described above. During burst-suppression, the 1 min analysing window is used over the whole frequency range to avoid the fluctuation of the output value. Finally, the entropy values are transformed according to a spline function to make the algorithm more sensitive in the region of interest for anesthesiologists. As in several above described algorithms, careful artifact rejection is performed before analysis. The entropy algorithm is made public and is described in [25].

In several studies the ability of state entropy and response entropy to monitor depth of anesthesia has been tested. In [27], for example, it has been found that, unlike BIS, the entropy parameters behave monotonously during burst suppression. Also, compared to BIS, the response entropy reacts earlier to the emergence from anesthesia. However, the study presented in [28] showed that the entropy measures are not sensitive to the loss of consciousness with nitrous oxide.

5. DISCUSSION

While the early EEG monitors were confined to display common amplitude and frequency domain variables of the signal, most modern methods apply complex signal analysis and output a single value (or a couple of values).

Probably influenced by BIS, the output of all recently developed methods is scaled between 0 and 100.

The methods involve both frequency domain and time domain analysis. In the majority of the algorithms the former one is based on power spectrum, thus losing the phase information, i.e., the information involved in waveforms – an important part of EEG analysis. Time domain analysis is used in detecting the burst suppression pattern and calculating the burst suppression ratio. EEG during suppression is actually far from a “straight line” but this fact is omitted by all systems due to practical signal-to-noise ratio restrictions. Bursts are often highly non-stationary but this, too, is omitted in calculating their power spectrum in some devices. The electrode locations are selected on practical grounds and EMG of frontal muscles is, so far, separated only on the basis of frequency content, although EMG and EEG overlap here. Most of the devices use only one recording channel. PSI is an exception, exploiting coherence between channels.

From the point of view of methodology, the algorithms can be divided into two groups: 1) methods involving feature extraction and subsequent discriminant analysis (ADAM, PSI, Narcotrend), and 2) methods based on specific methods, optimized to indicate depth of anesthesia (BIS, Entropy).

An important question seems to be: does the usage of non-linear methods give any advantage in monitoring anesthesia? The majority of recently developed methods apply some kind of non-linear analysis: BIS and PSI exploit bispectral analysis while Narcotrend and the Entropy Monitor exploit spectral entropy. In [17] Miller et al. come to the conclusion that the SynchFastSlow measure, calculated on the bispectral domain and used in the BIS monitor, does not contribute significantly to the final index. Spectral entropy, on the other hand, although involving non-linearity, is purely based on the power spectrum and does not take into account the phase of the signal. Several methods for testing the non-linearity of a signal (and thus the advantage of using non-linear methods) have been developed. Probably the most popular among these is the Tsay’s test [29]. Study of the non-linear behaviour of the EEG during deepening anesthesia still remains to be performed.

6. FUTURE PERSPECTIVES

All the above-mentioned drawbacks can be overcome. We can therefore look forward to further improvements. These will include detection of non-linearities such as reactions to stimuli, and possibly even to event related potentials. The systems so far try to cope with the fairly large variety of EEG patterns induced by different drugs and their combinations; in the future more drug specific solutions may be expected. Also, information from other physiological signals such as ECG and beat to beat heart rate is likely to be incorporated as well as information about the patient history, age, etc. Monitoring is likely to be extended to postoperative period and wireless technologies will be applied.

In the ICU, the need for monitoring depth of sedation is even more important than depth of anesthesia in OR [30]. The complexity of the problem, however, is higher here as the patients frequently have diseases affecting their brain function. The EEG during light sedation is more variable than in surgical anesthesia also due to different drugs and their combinations. Combination of evoked EEG responses and event related potentials with spontaneous EEG is important. Sleep patterns as well as epileptic disorders must be accounted for. The diagnosis, such as status epilepticus or cardiac arrest, influence the sedative treatment and should be taken into account in brain monitoring. Numerous studies show that ischemia and hypoxia, the most common causes of brain dysfunction in ICU, can be detected from the EEG signal before clinical signs appear and in a stage where the process is still reversible [30]. Also, the signs of recovery of the central nervous system appear in the EEG before any clinical signs can be detected.

It is well known that the mechanisms of the drug effect are different for different anesthetic and sedative drugs. It has recently been shown that the EEG during burst-suppression level propofol anesthesia contains specific patterns – sharp waves and spindles [31,32]. In [33] we showed that the activity, underlying these patterns, actually sets in long before EEG becomes suppressed although it is difficult to detect from scalp electrodes. We envisage that the future brain function monitor will be intelligent enough to take into account the information contained in these drug-dependent patterns. As new discoveries are made, interpretation of the physiological phenomena underlying these patterns will be incorporated. Also, the usage of brain function monitors in the ICU and emergency department require that not only the drug effects but also the state of the brain (ischemia, hypoxia) should be taken into account. The future monitor could be an interactive device to which the anesthesiologist feeds various clinical information and the monitor outputs several indices corresponding to sedation, hypnosis, hypoxia, ischemia, etc. The monitor can also warn the physician and point out critical findings in the signal.

ACKNOWLEDGEMENT

Writing this review has partly been supported by Estonian Science Foundation (grant No. 5625).

REFERENCES

1. Sharbrough, F., Chatrian, G.-E., Lesser, R. P., Lüders, H., Nuwer, M., and Pictor, T. W. American Electroencephalographic Society Guidelines for Standard Electrode Position Nomenclature. *J. Clin. Neurophysiol.*, 1991, **8**, 200–202.
2. Jääntti, V., Yli-Hankala, A., Baer, G. A., and Porkkala, T. Slow potentials of EEG burst suppression pattern during anaesthesia. *Acta Anaesth. Scand.*, 1993, **37**, 121–123.
3. Vanhatalo, S., Holmes, M. D., Tallgren, P., Voipio, J., Kaila, K., and Miller, J. W. Very slow EEG responses lateralize temporal lobe seizures: an evaluation of non-invasive DC-EEG. *Neurology*, 2003, **60**, 1098–1102.

4. Lipping, T., Loula, P., Jäntti, V., and Yli-Hankala, A. DC-level detection of burst-suppression EEG. *Methods Inf. Med.*, 1994, **33**, 35–38.
5. Kissin, I. General anesthetic action: an obsolete notion? *Anesth. Analg.*, 1993, **76**, 215–218.
6. Maynard, D. and Prior, P. Device for continuous monitoring of cerebral activity in resuscitated patients. *Br. Med. J.*, 1969, **4**, 545–546.
7. Maynard, D. Development of the CFM: the cerebral function analyzing monitor (CFAM). *Ann. Anaesth. Française*, 1979, **20**, 253–255.
8. CFAM brain monitors. <http://www.cfams.com>
9. Edmonds, H. L. and Paloheimo, M. Computerized monitoring of the EMG and EEG during anesthesia. An evaluation of the anesthesia and brain activity monitor (ABM). *Int. J. Clin. Monit. Comput.*, 1985, **1**, 201–210.
10. Thomsen, C. E., Rosenfalck, A., and Norregaard-Christensen, K. Assessment of anaesthetic depth by clustering analysis and autoregressive modeling of electroencephalograms. *Comput. Methods Programs Biomed.*, 1991, **34**, 125–138.
11. Thomsen, C. E. *Hierarchical Cluster Analysis and Pattern Recognition Applied to the Electroencephalogram – Development of ADAM (Advanced Depth of Anaesthesia Monitor)*. PhD Thesis, University of Aalborg, 1992.
12. Thomsen, C. E. and Prior, P. Quantitative EEG in assessment of anaesthetic depth: comparative study of methodology. *Br. J. Anaesth.*, 1996, **77**, 172–178.
13. Rampil, I. J. A primer for EEG signal processing in anesthesia. *Anesthesiology*, 1998, **89**, 980–1002.
14. Barr, G., Jakobsson, J. G., Owall, A., and Anderson, R. E. Nitrous oxide does not alter bispectral index: study with nitrous oxide as sole agent and as an adjunct to i.v. anaesthesia. *Br. J. Anaesth.*, 1999, **82**, 827–830.
15. Hirota, K., Kubota, T., Ishihara, H., and Matsuki, A. The effects of nitrous oxide and ketamine on the bispectral index and 95% spectral edge frequency during propofol-fentanyl anaesthesia. *Eur. J. Anaesth.*, 1999, **16**, 779–783.
16. Davidson, A. J. and Czarnecki, C. The bispectral index in children: comparing isoflurane and halothane. *Br. J. Anaesth.*, 2004, **92**, 14–17.
17. Miller, A., Sleigh, J. W., Barnard, J., and Steyn-Ross, D. A. Does bispectral analysis of the electroencephalogram add anything but complexity? *Br. J. Anaesth.*, 2004, **92**, 8–13.
18. Loomis, A. L., Harvey, E. N., and Hobart, C. A. Cerebral states during sleep as studied by human brain potentials. *J. Exp. Psychol.*, 1937, **21**, 127–144.
19. Schultz, B., Schultz, A., and Grouven, U. Sleeping stage based systems (Narcotrend®). In *New Aspects of High Technology in Medicine 2000* (Bruch, H.-P., Kockerling, F., Bouchard, R., and Schug-Pab, C., eds.). Monduzzi Editore, Bologna, 2000, 285–291.
20. Kreuer, S., Biedler, A., Larsen, R., Altmann, S., and Wilhelm, W. Narcotrend monitoring allows faster emergence and a reduction of drug consumption in propofol-remifentanyl anesthesia. *Anesthesiology*, 2003, **99**, 34–41.
21. Schmidt, G. N., Bischoff, P., Standl, T., Jensen, K., Voigt, M., and Schulte am Esch, J. Narcotrend® and Bispectral Index® monitor are superior to classic electroencephalographic parameters for the assessment of anesthetic states during propofol-remifentanyl anesthesia. *Anesthesiology*, 2003, **99**, 1072–1077.
22. Drover, D. R., Lemmens, H. J., Pierce, E. T., Plourde, G., Loyd, G., Ornstein, E., Prichep, L. S., Chabot, R. J., and Gugino, L. Patient state index: titration of delivery and recovery from propofol, alfentanil, and nitrous oxide anesthesia. *Anesthesiology*, 2001, **97**, 82–89.
23. Gan, T. J., Glass, P. S., Windsor, A., Payne, F., Rosow, C., Sebel, P., and Manberg, P. BIS utility study group: bispectral index monitoring allows faster emergence and improved recovery from propofol, alfentanil, and nitrous oxide anesthesia. *Anesthesiology*, 1997, **87**, 808–815.
24. Willmann, K., Springman, S., Rusy, D., and Daily, E. A preliminary evaluation of a new derived EEG index monitor in anesthetized patients. *J. Clin. Monit. Comput.*, 2002, **17**, 345–350.

25. Viertiö-Oja, H., Maja, V., Särkelä, M., Talja, P., Tenkanen, N., Tolvanen-Laakso, H., Paloheimo, M., Vakkuri, A., Yli-Hankala, A., and Meriläinen, P. Description of the Entropy™ algorithm as applied in the Datex-Ohmeda S/5™ entropy module. *Acta Anaesth. Scand.*, 2004, **48**, 154–161.
26. Särkelä, M., Mustola, S., Seppänen, T., Koskinen, M., Suominen, K., Juvonen, T., Tolvanen-Laakso, H., and Jäntti, V. Automatic analysis and monitoring of burst suppression in anesthesia. *J. Clin. Monit. Comput.*, 2002, **17**, 125–134.
27. Vakkuri, A., Yli-Hankala, A., Talja, P., Mustola, S., Tolvanen-Laakso, H., Sampson, T., and Viertiö-Oja, H. Time-frequency balanced spectral entropy as a measure of anesthetic drug effect in central nervous system during sevoflurane, propofol, and thiopental anesthesia. *Acta Anaesth. Scand.*, 2004, **48**, 145–153.
28. Anderson, R. E. and Jakobsson, J. G. Entropy of EEG during anaesthetic induction: a comparative study with propofol or nitrous oxide as sole agent. *Br. J. Anaesth.*, 2004, **92**, 167–170.
29. Tsay, R. S. Nonlinearity tests for time series. *Biometrika*, 1986, **73**, 461–466.
30. Jordan, K. G. Continuous EEG monitoring in the neuroscience intensive care unit and emergency department. *J. Clin. Neurophysiol.*, 1999, **16**, 14–39.
31. Jäntti, V., Mustola, S., Huotari, A. M., and Koskinen, M. The importance of looking at the EEG when presenting univariate variables to describe it. *Br. J. Anaesth.*, 2002, **88**, 739.
32. Huotari, A. M., Koskinen, M., Suominen, K., Alahuhta, S., Renu, R., Hartikainen, K. M., and Jäntti, V. Evoked EEG patterns during burst suppression with propofol. *Br. J. Anaesth.*, 2004, **92**, 18–24.
33. Lipping, T., Ferenets, R., Puumala, P., Suominen, K., Karvonen, E., Sonkajärvi, E., Alahuhta, S., Heikkinen, E., Erola, T., Baer, G., and Jäntti, V. EEG independent component and coherence analysis from scalp and depth electrodes during propofol anesthesia. In *Proc. 25th IEEE EMBS Annual International Conference*. Cancun, Mexico, 2003, 2471–2474.

Ülevaade EEG-signaali tööstlusest ajutegevuse seires anesteesia ja intensiivravi tingimustes

Tarmo Lipping ja Ville Jäntti

Anesteesia sügavuse hindamisel kliinilises töös on EEG viimaste aastate jooksul kujunenud “kuldseks standardiks”. On välja töötatud mitmeid EEG-signaali tööstlusele põhinevaid monitore, mis esitavad graafiliselt “anesteesia sügavuse” indeksi. Neid meetodeid on kasutatud miljonite patsientide seires. Artiklis käsitletakse kõigepealt anesteesia sügavusega seotud mõisteid ning seejärel antakse ülevaade tuntumatest EEG-l baseeruvatest anesteesia seire meetoditest ja algoritmidest. Artikli lõpus tehakse kokkuvõtte kirjeldatud meetoditest ning visandatakse anesteesia seire arengusuunad.