Proceedings of the 28th IEEE
EMBS Annual International Conference
New York City, USA, Aug 30-Sept 3, 2006

Method for the Automatic Detection of Epileptiform Waveforms in Sevoflurane-induced Anesthesia EEG

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Abstract—**Sevoflurane is a volatile anesthetic which is reported to cause epileptiform EEG changes together with undesired symptoms such as convulsions. In this paper, an algorithm for the automatic detection of these EEG changes is presented which could enable safer induction of anesthesia with sevoflurane by informing the clinicians about the epileptiform EEG. EEG was recorded from 60 healthy female patients during sevoflurane anesthesia. A neurophysiologist classified the EEG waveforms. Each anesthesia period lasted 6 minutes. 48 signal features were extracted from the raw EEG. 5-sec segments of EEG were classified based on the extracted features using a decision tree with a logistic regression based decisions and the classification results were compared to the neurophysiologist's classifications. Awake EEG was recognized with 69% / 96% (sensitivity / specificity), Burst suppression with 56% / 98%, Epileptiform EEG with 83% / 87 %, normal slow anesthesia EEG with 86% / 64 %, slow anesthesia EEG with monophasic pattern with 65% / 80 %, and slow anesthesia EEG with monophasic pattern and spikes with 54% / 84%.**

I. Introduction

Sevoflurane is an ultra-short-acting volatile anesthetic. Hemodynamic stability and lack of respiratory irritation are some of its most important assets. The epileptiform EEG changes caused by sevoflurane anesthesia have been documented in many occasions [1] - [5]. Also external symptoms similar to epileptic seizures have been described [1] [6]. Because of these findings, several authors have expressed their concern over the use of sevoflurane [6] [2] [3]. For the safer use of sevoflurane, it would be beneficial to be able to monitor the EEG changes during anesthesia so that epileptic changes could be detected as early as possible.

The objective of this study was to develop a method for the automatic detection of epileptiform and other waveforms encountered during sevoflurane anesthesia. Because of the systematic EEG changes during deepening sevoflurane anesthesia, detection of different waveforms could give an early warning of upcoming undesired events, such as epileptic symptoms.

Manuscript received March 30, 2006.

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II. Methods

The data collection protocol has been described in detail earlier [1] but with a different number of patients included. EEG was recorded from 60 healthy women undergoing gynecologic surgery and receiving sevoflurane induced anesthesia. Each received a premedication of 5 mg of oral diazepam 60 minutes before the surgery. Each sevoflurane-nitrous oxide-oxygen mask anesthetic induction with 8% inspired sevoflurane lasted 6 minutes.

The EEG data were collected with four channels: Fp1-A1, Fp2-A2, Fpz-F7, and Fpz-F8 (International 10-20 system). The EEG was digitally collected with Aspect A-1000n EEG monitor (Aspect Medical Systems) with 128 Hz sampling frequency and passband of 1.0 Hz - 50 Hz. Every trial was completed without complications and none of the data were excluded.

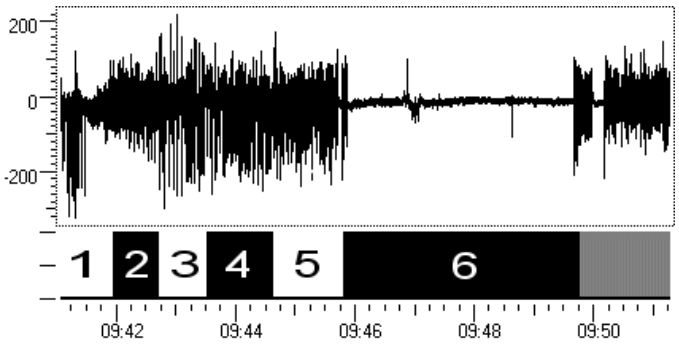

Fig 1 Example of an EEG recording. The annotated EEG waveforms are 1) awake 2) normal slow activity 3) abnormal slow activity 4) abnormal slow activity with spikes 5) PED 6) burst suppression. Period annotated with grey is excluded (post-anesthesia EEG).

The EEGs were classified with one second time resolution by a neurophysiologist familiar with anesthesia EEG. The electroencephalographic phenomena were classified as awake activity, normal slow activity (representing surgical level of anesthesia), abnormal slow activity (representing EEG with monophasic component), abnormal slow activity with spikes (representing EEG with signs of emerging epileptiform activity), periodic epileptiform discharges (PED), and burst suppression (BS). Examples of four selected waveforms are presented in Fig 2.

The changes in EEG during anesthetic induction in this study followed a certain pattern. The eye blink artefacts disappeared rapidly after the beginning of induction. After that there was a short period of increased beta activity with slow eye movements. The delta activity began to evolve next. In 9 patients, no epileptiform activity was detected and different slow activities alternated until the end of the induction. In other patients, epileptiform activity was detected. In 17 patients, after epileptiform activity burst suppression pattern emerged and lasted until the end of induction. An example of an EEG recording together with its annotations is shown in Fig 1.

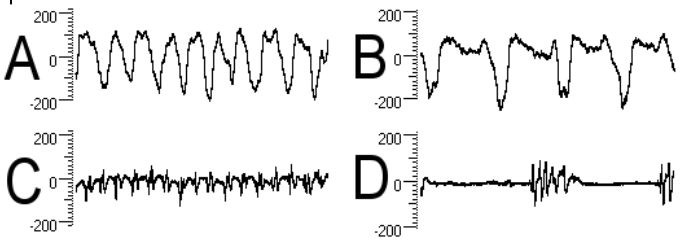

Fig 2 Examples of selected waveforms. A) Normal slow activity, B) Abnormal activity, C) Periodic epileptiform discharges, D) Burst suppression. Each sample is 10 sec long. Vertical axis is in millivolts.

48 signal features were extracted from 5-second EEG segments. The features are listed in Table 1. It was visually confirmed that all four channels contained approximately the same information and thus for each case the least artefact-contaminated channel was chosen for feature calculations. Three different groups of features were extracted (wavelet decomposition features, power spectrum features and those based on raw EEG). The calculations for most of them are trivial. The formulas for the rest are briefly described.

A 5-level wavelet decomposition was made for each 5-second EEG segment using Daubechies 3 wavelet. Statistical properties (standard deviation, skewness, and kurtosis) were calculated from the obtained wavelet detail coefficients d_i separately for each decomposition level. Coefficient entropy H was calculated separately for each decomposition level j as

$$H_j = -\frac{\sum_{i=1}^{N} \tilde{d}_i \cdot \log_2(\tilde{d}_i)}{\log_2(N)} \quad \text{where} \quad \tilde{d}_i = \frac{d_i^2}{\sum_{i=1}^{N} d_i^2} \qquad (1)$$

where N represents the number of detail coefficients of the decomposition level. The wavelet entropy calculation bears some similarities with the subband wavelet entropy described, e.g., in [7]. However, in our calculation the wavelet entropy of each band is independent of the others. Each of them is also normalized to the interval [0, 1] making them independent of the scale of EEG.

Spectral peak power is the power of the highest peak in power spectrum (PSD). Spectral peak frequency is the frequency of the highest peak in PSD. Spectral edge frequencies 95% and 50% are the frequencies below which 95% and 50%, respectively, of the power of EEG is located in PSD.

Spectral entropy S_N for a frequency band $[f_1, f_2]$ is defined similarly as for example in [8]:

$$S_N(f_1, f_2) = \frac{-\sum_{f_i=f_1}^{f_2} P(f_i)\log(P(f_i))}{\log(N[f_1, f_2])} \qquad (2)$$

where $P(f_i)$ represents the PSD value of the frequency f_i. The PSD values are normalized so that their sum in the band $[f_1, f_2]$ is one. $N[f_1, f_2]$ is the number of frequency components in the corresponding band in PSD.

For classification, a decision tree approach was used. The classification problem of multiple classes was divided into binary decisions as depicted in Fig 3. The structure of the tree was decided based on the properties of the different waveforms and their clinical meaning.

For the detection of burst suppression, a method based on non-linear energy operator described in [8] was used.

For the other decisions, following procedure was applied in generating the rules for each of them. First stepwise regression analysis was used to extract those features correlating the most with the decision at hand. Using the obtained set of variables, a logistic regression classifier was trained for the specific decision. Only data from those classes that were involved in each decision were used in their training.

Features from raw EEG
Mean amplitude
Median amplitude
Root mean square amplitude
Peak-to-peak amplitude
Features from 5-level wavelet decomposition
Standard deviation of coefficients
Skewness of coefficients
Kurtosis of coefficients
Coefficient entropy
Features from power spectrum
Spectral peak power
Spectral peak frequency
Spectral edge frequency 95%
Spectral edge frequency 50%
Spectral entropy
Power (8.2- 20 Hz) / Power(1.0-8.0 Hz)
Spectral entropies, relative powers, and absolute powers of the bands 1.0-3.8 Hz, 4.0-8.0 Hz, 8.2-13.0 Hz, 13.2-20.0 Hz, 20.2-47.0 Hz, and 1.0-50.0 Hz

Table 1 Extracted EEG signal features. Each feature is calculated from a 5-sec EEG segment.

The output of each logistic regression decision was a value between 0 and 1 and it was considered a probability indicating the reliability of the decision. Using these probabilities, a probabilistic model was created where for each EEG segment the probability of belonging to a particular class is the product of the conditional probabilities of every earlier decision. That is,

$$P(A \cap A_2 \cap \cdots \cap A_n) = P(A_1 | A_2 \cap \cdots \cap A_n) \cdot P(A_2 | A_3 \cap \cdots \cap A_n) \cdots P(A_{n-1} | A_n) \cdot P(A_n) \quad (3)$$

For example, calculating the probability of a certain EEG segment belonging to e.g. the class "PED" would require the calculation of equation

$$\begin{aligned} P('PED') &= P('PED' \cap 'not\_BS' \cap 'not\_AWAKE') \\ &= P('PED' | 'not\_BS' \cap 'not\_AWAKE') \cdot \\ &\quad P('not\_BS' | 'not\_AWAKE') \cdot P('not\_AWAKE') \end{aligned} \quad (4)$$

With such an approach, a mistake in an earlier decision can still be corrected by the later decisions if they indicate strongly enough that the segment is belonging to a class other than indicated by the earlier decision.

Receiver operating characteristic (ROC) curves were used in tuning the threshold values for each logistic regression decision. This was done in order to balance especially the classification accuracies of those EEG waveforms that had fewer samples in the training data.

The data were randomly divided into training (30 patients) and validation sets (30 patients). The features and the threshold values of the decision tree were optimized with the training data. The results are calculated for the validation data.

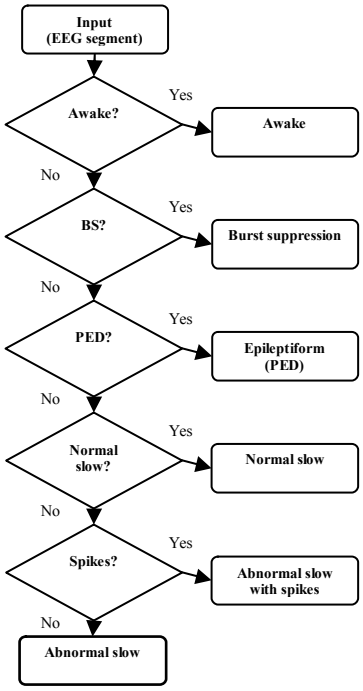

Fig 3 Decision tree structure for the classification of the EEG waveforms.

III. RESULTS

The classification results for each waveform for the validation dataset are presented in Table 2. In these results, the classification tree leaf with the highest probability has been considered the selected output.

Waveform	Sensitivity	Specificity
Awake	69 %	96 %
Burst suppression	56 %	98 %
PED	83 %	87 %
Normal slow	86 %	64 %
Abnormal slow	65 %	80 %
Abnormal slow with spikes	54 %	84 %

Table 2 Classification results for the validation dataset.

IV. CONCLUSIONS

A method for the automatic detection of different EEG waveforms during sevoflurane anesthesia is presented. The method can inform clinicians about the unwanted EEG waveforms and possibly give an early warning of upcoming undesired symptoms, such as convulsions.

There are reports suggesting that some anesthesia monitors do not function properly during anesthesia induced epileptiform EEG [9]. The presented method may also provide complementary information to the existing anesthesia monitors and thus improve their performance during such EEG patterns.

There is large inter-scorer variability in human experts' EEG classification. For example, Wilson & Emerson have concluded that EEG experts do not routinely achieve average recognition sensitivities of 80-90 % when concerning EEG spike detection [10]. From this point of view, many of the classification accuracies presented here are acceptable. Some of the detection accuracies suffer from inappropriate annotations. For example, burst suppression is clearly a composition of two distinct patterns (bursts and suppressions) which should be separately annotated and detected in order to improve the detection accuracy.

The method will be next adjusted with different EEG datasets and also its applicability to the detection of other abnormal waveforms will be examined.

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