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Classification of EEG Bursts in Deep Sevoflurane, Desflurane and Isoflurane Anesthesia Using AR-modeling and Entropy Measures

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***Abstract*— A study relating signal patterns of burst onsets in burst suppression EEG to the anesthetic agent or anesthesia induction protocol is presented. A dataset of 82 recordings of sevoflurane, isoflurane and desflurane anesthesia underlies the study. 3 second segments from the onset of altogether 3214 bursts are described using AR model parameters, spectral entropy and sample entropy as features. The features are clustered using the K-means algorithm. The results indicate that no clear cut distinction can be made between the burst patterns induced by the mentioned anesthetics although bursts of certain properties are more common in certain patient groups. Several directions for further investigations are proposed based on visual inspection of the recordings.**

I. Introduction

Burst suppression (BS) pattern in the EEG signal is defined as alternating periods of suppressed EEG and high amplitude mixed frequency bursts. Commonly amplitudes below 5 microvolts for at least a 2 second period is considered as a definition for EEG suppression. Burst suppression appears in the case of severe brain injury or hypoxia, but also in deep anesthesia with all commonly used anesthetic agents. In the latter case the condition is totally reversible. Most commercially available depth-of-anesthesia monitors detect burst suppression pattern assessing the depth of anesthesia at this state as the ratio of time of suppressed EEG to that of bursts in a sliding window. The variable is called burst suppression ratio.

Various properties as well as the mechanism behind the BS pattern have been studied by several authors. Lipping et. al. have shown that the dynamics of the BS is different in enflurane and isoflurane anesthesia with relatively more frequent bursting and shorter bursts in the case of enflurane [1]. Huotari et. al. have found that bursts can be invoked during suppression by electrical stimulus and that the invoked bursts have typical waveform properties not seen in spontaneous bursts [2]. Steriade et. al. have studied the role and mechanisms of the cortico-thalamic neural loops in the genesis of BS as well as EEG spindles accompanying BS in the case of certain drugs [3, 4]. In gradually deepening anesthesia the BS pattern is usually preceded by high amplitude slow waves and it has been suggested that these waves are a manifestation of up and down switching of the electrical state of the cortex. EEG suppression follows when the cortex 'gets stuck' to the upper state. This hypothesis is confirmed by the finding that bursts actually occur on a DC-level shift not usually observed due to the high-pass prefiltering of the EEG signals in common clinical practice [5].

Although usually appearing as a clear on-off phenomenon, it is occasionally difficult to determine where exactly a burst starts or ends. Also, the waveform of bursts varies significantly depending on the anesthetic agent but also from recording to recording in the case of the same drug and even within a single recording. The dataset underlying the present study - 82 recordings of the whole anesthesia procedure with three different drugs and different induction protocols - gave us a good opportunity to study the burst waveforms. Visual analysis of the recordings indicated that several typical burst patterns could be observed. However, no clear correlation between the burst patterns and the administered drug or induction protocol could be visually observed. The aim of this study is to use unsupervised classification methods to classify the burst patterns according to their spectral properties and waveform complexity. We also study if correlation between the burst properties and the administered drug or type of induction can be shown.

II. Material

The data set underlying this study contains 82 recordings of the whole anesthesia procedure including induction, period of deep anesthesia with BS EEG and withdrawal of the drug until the patient was fully awake. The study was approved by the Ethics Committee of the Silesian University of Medicine, Katowice, Poland (approval no. NN-6501-196/06). Anesthesia was maintained using three different inhalation anesthetics: sevoflurane, isoflurane (ISO) and desflurane (DES). In the case of sevoflurane three different induction methods were applied; in the first group propofol was used for induction (SEVO), in the second group volatile induction was performed with the single breath technique (Vital Capacity Rapid Inhalation Induction; SEVO-VCRII) while in the third group conventional spontaneous inhalation induction was used (SEVO-VIMA).

The EEG signal was recorded using S/5 Compact Anesthesia Care Monitor (GE Healthcare) with S5/Collect software (Datex-Ohmeda Division of Instrumentarium Corporation). Raw EEG data includes 4 channel EEG (100

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Hz sampling frequency) plus an additional channel measured from the forehead using the Entropy™ sensor (400 Hz sampling frequency). In this study only the entropy sensor channel was used.

The recordings were visually analyzed and the burst onsets were marked. In several occasions the exact burst onset time was difficult to detect; patterns similar to the beginning of a burst were seen during continuous EEG together with segments of somewhat suppressed EEG. In the annotation of burst onsets the goal was to find representative signal patterns, therefore the cases where burst onsets were difficult to determine were discarded. Also, the bursts had to last for at least 3 seconds after the onset for reliable analysis, therefore in some recordings several short bursts had to be discarded as well. In 13 of the 82 recordings no BS was observed. The remaining recordings were divided between the five groups as follows:

- SEVO: 8 recordings with 445 bursts
- SEVO-VIMA: 16 recordings with 852 bursts
- SEVO-VCRII: 13 recordings with 447 bursts
- ISO: 15 recordings with 801 bursts
- DES: 17 recordings with 627 bursts.

III. Methods

The EEG signals were first prefiltered using an equiripple FIR filter to reject 50 Hz power noise and discard frequencies above 99 Hz. Three second segment from the beginning of each burst was used in the analysis. According to visual analysis the burst patterns differed in their frequency content; some bursts started with high frequency (up to 20 Hz) activity while the frequency content of other bursts seemed to be limited to below 10 Hz. Therefore we chose AR modeling as the primary method to extract features for clustering and classification. We also checked if signal entropy measures such as sample entropy and spectral entropy added any discriminative power to classification. The conventional K-means clustering and classification algorithm was used for classification. Although the K-means algorithm does not usually find the optimal solution, its performance is simple and intuitive; therefore it was considered as a suitable choice for this kind of preliminary study. In the following we give a short description of the K-means classifier as well as the entropy algorithms.

A. K-means classifier

The data are clustered according to the following iterative procedure:

1. determine randomly K class centers in N-dimensional feature space
2. calculate the distance from each data point to each class center
3. allocate each data point to the class of the closest center to it
4. recalculate the class centers as the mean of the data points allocated to the particular class
5. repeat the algorithm until the change in the location of the class centers remains under predetermined threshold.

In the second phase of the algorithm individual data points are reassigned and the sum of distances between the data points to their respective class centers is calculated. If the sum of distances is decreased, the reassignment is preserved. In this study the MATLAB *kmeans* routine was used to perform the classification.

B. Spectral entropy

Spectral entropy measure (SpEn) is based on the definition of entropy given by Claude Shannon:

$$y = -\sum_i x_i \log x_i.$$

In the calculation of spectral entropy the function is applied to the normalized power spectrum of the signal, P_i, where i is the frequency value in the power spectrum. The power spectrum is normalized so that the sum over all frequency values equals to one. The spectral entropy measure is calculated as:

$$SpEn = \frac{-\sum_{i=f_l}^{f_h} P_i \log P_i}{\log M},$$

where f_l and f_h are the lowest and highest frequency values used in the calculation and M is the total number of frequency bins in the corresponding frequency range. Spectral entropy was first applied to EEG signal analysis by Inouye et. al. [6] and it is the main component of the commercially available Entropy™ index for the assessment of anesthetic depth.

C. Sample entropy

Sample entropy (SampEn) is a modification of the approximate entropy measure introduced by Pincus [7]. From the signal s of length N, $(N-m+1)$ vectors of length m are formed: $\boldsymbol{x}_m(i) = \{s(i), s(i+1) \dots s(i+m-1)\}$. After that, for each $i, 1 \le i \le N-m+1$ the quantity $C_i^m(r)$ is calculated using:

$$C_i^m(r) = \frac{\text{number of } j \text{ such that } d[\boldsymbol{x}_m(i), \boldsymbol{x}_m(j)] \le r}{N-m+1},$$

where the distance d between the vectors $\boldsymbol{x}_m(i)$ and $\boldsymbol{x}_m(j)$ is defined as:

$$d[\boldsymbol{x}_m(i), \boldsymbol{x}_m(j)] = \max_{k=1,2,\dots,m} (|s(i+k-1) - s(j+k-1)|)$$

and r is the parameter of the algorithm referred usually as the filtering level. The summation

$$C^m(r) = \frac{1}{N-m} \sum_{i=1}^{N-m} C_i^m(r)$$

is performed next and the sample entropy measure is obtained as

$$SampEn(m, r, N) = -\ln \frac{C^{m+1}(r)}{C^m(r)}.$$

r is most commonly set to 0.2 times the standard deviation of the signal segment to be analyzed. In EEG analysis the dimension m is most often set to 2.

Approximate entropy and sample entropy are often used in EEG analysis in research. To our knowledge these methods are not applied in commercial equipment though.

IV. RESULTS

As the clustering performance is crucial for studying the correlation between burst properties and the administered drugs or induction protocols, we first analyzed different sets of features and feature space dimensionalities. The results are presented in Fig. 1. Three kinds of feature sets were used: 1) AR-model parameters with AR-model order from 4 to 13; 2) AR-model parameters of model orders 3 to 12 together with sample entropy and 3) AR-model parameters of model orders 2 to 11 together with sample entropy and spectral entropy. The feature values were normalized to zero mean and unit variance before applying the K-means classification to give each feature potentially equal discriminative power. As could be expected, the total sum of distances from the data points to corresponding cluster centers increases with the dimensionality of the feature space. It can be seen from the figure that the entropy measures do not add to the clustering performance of the K-means algorithm when compared at similar dimensionality. Based on the analysis the feature space of AR model parameters of order 7 was selected for further consideration.

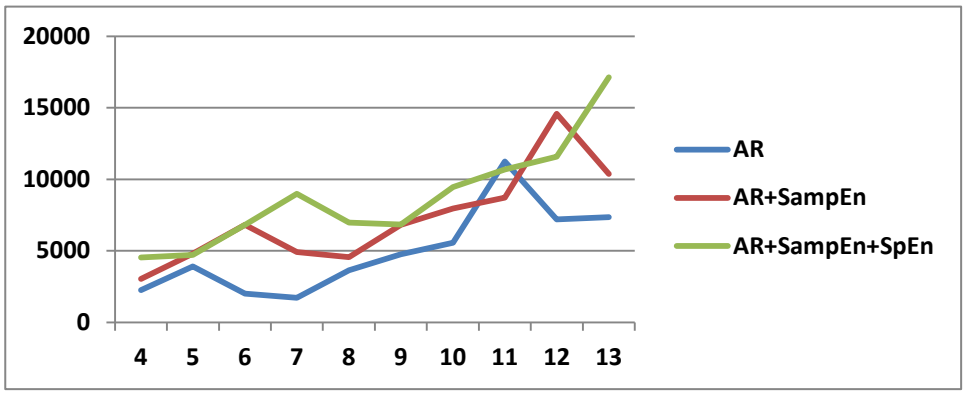

Figure 1. Clustering performance using various feature sets and feature space dimensionalities. The vertical axis represents the total sum of distances from data points to corresponding cluster centers. The horizontal axis represents the dimensionality of the feature space.

For curiosity we also calculated the distribution of the data points on the SampEn - SpEn two-dimensional feature space. The results are shown in Fig. 2. It can be seen that no clear clusters are formed in this feature space. As could be expected, there is a positive correlation between the two entropy measures. Sample entropy seems to capture the properties of the bursts better that spectral entropy as the variance along the horizontal axis is higher.

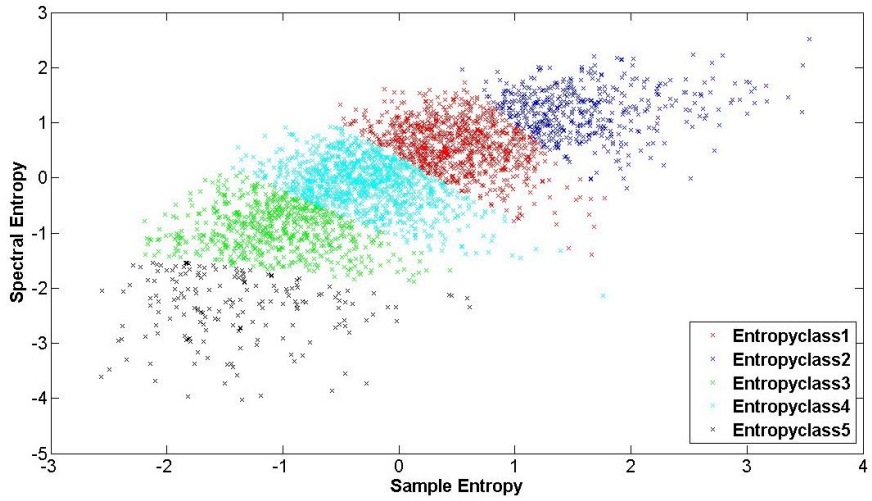

Figure 2. Distribution of the bursts on the SampEn - SpEn feature space and corresponding K-means classification results. The classes here are not the same as in Fig. 3 and Fig. 4. The entropy measures are normalized to zero mean and unit variance

As the recordings were originally allocated to five groups according to the anesthetic drug and induction protocol, we also used five classes in the K-means algorithm. The dimension of the feature space was 7 and only the AR model parameters were used as features based on the conclusions from Fig. 1. Fig. 3 shows the correlation between the classes determined by the K-means algorithm and the patient groups. In Fig. 4 example bursts from the five classes

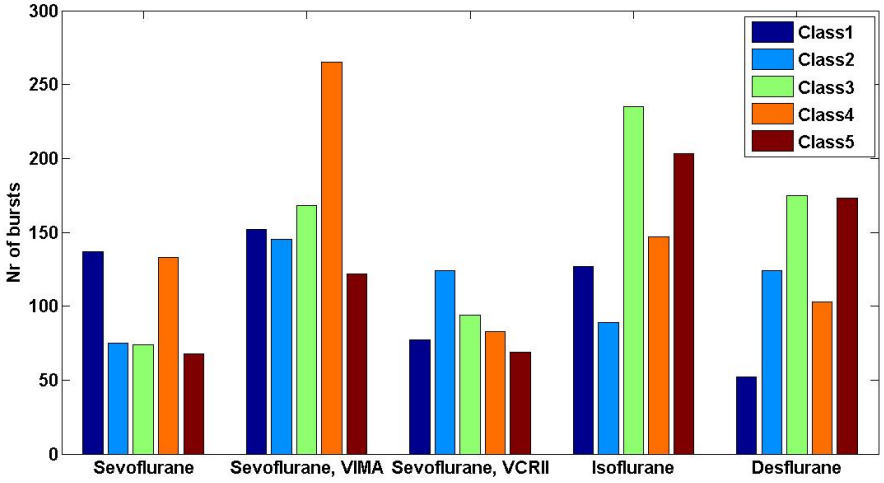

Figure 3. Correlation between the classes determined by the K-means classifier and the administered anesthetic drug or induction protocol.

are presented. The cases yielding features closest to the cluster centers were chosen for Fig. 4.

Fig. 4 indicates that although the clustering algorithm has succeeded to differentiate between different burst waveforms, the bursts of classes 3…5 still look quite similar. Visual analysis of the data presumes that more distinct classification is possible. Fig. 3 indicates that bursts belonging to the different classes can be found from each recording group. However, class 4 bursts are clearly overrepresented in the SEVO-VIMA group and class 5 bursts tend to be more common in ISO and DES groups.

V. Discussion and Conclusions

This study presents preliminary results of the attempt to relate burst waveforms to the administered anesthetic drug or induction protocol. Although no clear distinction could be made, certain classes of bursts dominated in certain patient groups. Some of the reasons our analysis could only poorly discriminate between the patient groups are:

1. the feature set does probably not capture the relevant properties of the bursts well. In the visual analysis the dynamics of signal properties within the first seconds of the burst is important. Our features were not able to take into account the non-stationarity of the signal
2. the K-means clustering algorithm does not yield the optimal solution; other algorithms like the Self Organizing Map should be tried
3. it is possible that the drugs used in our study yield similar burst patterns; the change of the burst properties during the recording might be more important than the drug used.

Visual analysis of burst patterns indicated that there are several other aspects of the BS phenomenon requiring further attention. As one of our previous studies showed, the dynamics of bursting, i.e., the lengths of bursts and suppression segments, is an important property of the phenomenon and differs in different patient groups [1]. Also, there is a hypothesis that burst dynamics depends on the age of the patient. Visual analysis shows that the pattern of the burst onset depends on the length of the preceding suppression segment - longer suppression segment usually causes more distinct burst onset. In some cases a typical wave or polywave is seen at the beginning of bursts. Future studies should also incorporate other drugs like propofol or etomidate, for example, and relate burst patterns to the models of burst mechanisms.

Studying the BS phenomenon - the dynamics of bursting, the burst waveforms and their evolution - has the potential application in brain monitoring in the operating room and intensive care unit.

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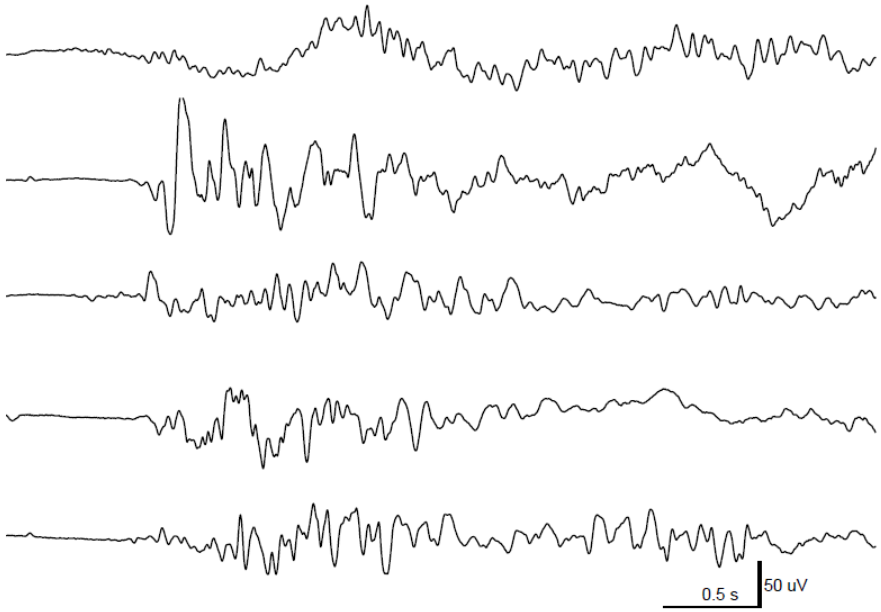

Figure 4. Examples of bursts of classes 1 (uppermost curve) to 5 (lowermost curve)