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On Separability of A-Phases during the Cyclic Alternating Pattern

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Abstract— A statistical analysis of the separability of EEG A-phases, with respect to basal activity, is presented in this study. A-phases are short central events that build up the Cyclic Alternating Pattern (CAP) during sleep. The CAP is a brain phenomenon which is thought to be related to the construction, destruction and instability of sleep stages dynamics. From the EEG signals, segments obtained around the onset and offset of the A-phases were used to evaluate the separability between A-phases and basal sleep stage oscillations. In addition, a classifier was trained to separate the different A-phase types (A1, A2 and A3). Temporal, energy and complexity measures were used as descriptors for the classifier. The results show a percentage of separation between onset and preceding basal oscillations higher than 85 % for all A-phases types. For Offset separation from following baseline, the accuracy is higher than 80 % but specificity is around 75%. Concerning to A-phase type separation, A1-phase and A3-phase are well separated with accuracy higher than 80, while A1 and A2-phases show a separation lower than 50%. These results encourage the design of automatic classifiers for Onset detection and for separating among A-phases type A1 and A3. On the other hand, the A-phase Offsets present a smooth transition towards the basal sleep stage oscillations, and A2-phases are very similar to A1-phases, suggesting that a high uncertainty may exist during CAP annotation.

I. INTRODUCTION

Analysis and interpretation of the cerebral information during sleep is an important task in clinics, as many pathologies and social problems are associated to sleep problems [1]. Sleep apnea, insomnia and metabolic syndrome are among the most common pathologies, which, in addition to social problems are correlated to sleepiness, tiredness, and lack of concentration produced by a low sleep quality [1].

The standard procedure to evaluate sleep is the polysomnography (PSG). The PSG consists in the recording of electroencephalogram (EEG), electrooculogram and electromyogram. This information is mainly used to evaluate the sleep stages (wake, 1-4 and REM). In addition, more signals such as electrocardiogram, airflow and pulsioxymetry are used to assess some pathologies [1]. Four decades ago,

Terzano et al. [2] observed and organized new information on the structure of the brain activity during normal and pathologic sleep. This structure consists in short cerebral oscillations that break the basal EEG rhythms of the sleep stages. Those oscillations are called A-phases and last between 2s and 60s. Fig. 1 shows an example of EEG signal during approximately 60 seconds of stage 2 sleep. The dashed line shows the A2-phases that are observed during this EEG segment. One can observe that there exist changes in frequency and amplitude of the EEG during each A-phase.

A-phases are classified in three groups based on the observed frequency information:

- A1-phase. It is characterized by bursts and k-complexes of Delta waves (0.5 Hz - 4 Hz).

- A2-phase. It has rapid EEG waves that cover between 20% and 50% of the A-phase duration

- A3-phase. It is characterized by Alpha (8 Hz - 12 Hz) and Beta waves (12 Hz - 30 Hz), which cover more than 50% of the A-phase duration.

The standard procedure to annotate A-phases, from an EEG recording, is by visual inspection; however, there exists a high inter-scorer variability [3]. In order to reduce the scoring time and to alleviate the inter-scorer variability, some studies have presented interesting automatic algorithms with good performance [4-5]. Their main focus is in detecting A-phases based on changes of EEG characteristics. However, most of them need improvement localizing the onset and offset of the A-phase. In addition, it is interesting to analyze the feasibility of automatically discriminating between the three types of A-phases, as defined by an expert physician. Such a study may also help to understand the extent of the overlap between the fingerprints of different types of A-phases.

The goal of the study is to evaluate the feasibility in separating the Onset and Offset of the A-phases with respect to the basal oscillations of the non-REM (NREM) sleep stages, and evaluate the separability of the different A-phase types in healthy subjects. The separability is measured based on the performance of the k-Nearest Neighbors (kNN) algorithm [6]. This algorithm is fed with statistical, complexity and frequency information obtained from the EEG signal during the NREM sleep basal oscillation and the A-phases.

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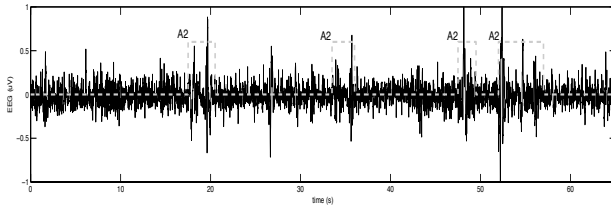
Fig. 1 EEG segment during the sleep phase 2. Dashed line shows A2-phases.

II. METHODOLOGY

A. Protocol

Five healthy adult subjects, 2 males and 3 females, of ages between 25 and 45 years (mean 32.7 yrs) underwent the study. The sleep polysomnographic recordings were acquired and annotated at the Parma University Sleep Disorders Center. Sleep analysis was carried out after one adaptation night. Sleep stage annotations and CAP scoring were done by sleep experts, following the standard procedure of R&K rules (sleep stages every 30s) while CAP scoring was based on published guidelines [2]. A single unipolar EEG derivation per subject was used for this analysis, either C3-A2 or C4-A1. The signal was sampled at 100 Hz, and bandpass-filtered at 0.3 Hz - 40 Hz.

B. Segments and features for background and onset-offset separation

For each A-phase defined by the expert, the following windows are compared: 1) 2s before the onset, 2) 2s after onset, 3) 2s before offset and 4) 2s after offset. In addition to the common types of A-phases, we separated the A1-phase in two types, thus finally we have the following groups: 1) A1-phase during sleep stage 2, 2) A2-phase during NREM sleep 3) A3-phase during NREM sleep and 4) A1-phase during sleep stage 3-4. Note that sleep stage 1 was not considered in this study due to its low occurrence. We can define the whole set as, $C_{i,j} = \{a_j | a_j \epsilon A_i\}$ where $i=1, 2, 3$ and 4 represents the activation group and $j=1, 2, 3$ and 4 is the segment around the onset or offset. The duration of two seconds for each segment is selected due to the minimum duration of A-phases and the minimum separation between A-phases. A1-phase was separated in two groups since one can find many A1-phases during light and deep sleep but the basal EEG oscillations are completely different between those sleep stages.

For each segment: mode, standard deviation, skewness, kurtosis, energy and the power after spectral decomposition in 4 bands (Delta, Theta, Alpha and Beta) of the EEG were computed. In addition, complexity measurements are computed from the whole night EEG in sliding windows of 4s with 2s of overlapping. The values of segments related to the C set are used as features. The complexity measurements were: Lempel-Ziv Complexity, Sample Entropy, Fractal Dimension and Tsallis Entropy. A total of 2211 A-phases are analyzed in the study with A_1=519, A_2=459, A_3=372 and A_4=881.

C. Feature extraction for A-phase separation

The same features, described in section II.B, are used for A-phase type separation. In addition to these features, A-phase duration is also included. Note that the features are computed for the whole A-phase duration and here the A1-phase group includes phases from sleep stages 1 and 3-4. Thus, we have 3 classes: A1, A2 and A3.

D. Feature selection and classifier

There are many methods to find the best decision boundary that separates two or more groups based on the their characteristics or features. Among the most used, we can find the k-Nearest Neighbors (kNN) algorithm. kNN is used due to its simplicity and ability to find complex decision boundaries.

The kNN computes the *a posteriori* probability that a sample $x_{new} \in \mathbb{R}^n$, (where n is the number of features) belongs to a group g_i. This is evaluated based on the proportion data points belonging to g_i from a sample consisting of the k data points closest to x_{new}:

$$P(g_i | x_{new}) = \frac{k_i}{k} \tag{1}$$

i stands for the *i-th* group, $k_i \leq k$ is the number of data points (from the k nearest neighbors) belonging to group g_i

Feed-forward selection procedure with Leave-One-Out crossvalidation were used for feature selection and to choose the best k, where k={1,3, …, 27}. The procedure can be summarized as follows: for each subject, the feature vectors corresponding to the A-phases (pre-onset, post-onset, pre-offset and post-offset) of that subject are classified using data from the other four subjects as training samples; accuracy, sensitivity and specificity measures were computed for each subject, and then averaged across all five subjects, in order to evaluate the overall performance of the classifier. This methodology is used to evaluate the separation between background activity and A-phases during both the onset and the offset of the A-phases, and also for A-phase type classification.

III. RESULTS

Separability of A-phases among types and Onset-Offset with respect to the basal EEG oscillations is presented. The first part of the results focus in the Onset-Offset separability while the second part is about type separation.

Several tests were performed using different combinations of features. Here we present the results obtained with the combination of proposed features that yielded the best performance. These features are: a) for onset-offset A-phase separation, the most common features in the different groups were {standard deviation, Power in Delta bad, Lempel-Ziv complexity, TSA, Energy}, b) for separation among different A-phases type, the most common features were {Sample Entropy, standard deviation, Lempel-Ziv complexity, Energy, Power in Beta band}.

A. Onset-Offset separation

Table I shows the performance of the kNN algorithm in separating basal EEG oscillations and Onset A-phase. A1-phase during sleep stage 2 shows the best results: accuracy around 94% is achieved. The worst case is A1-phase during sleep stage 4, with accuracy close to 87%. In addition, A1-phase during sleep stage 4 shows a higher variance in the classification.

The Offset A-phase separation with respect to the basal EEG oscillations is shown in Table II. Again, the best case is obtained for A1-phase during sleep stage 2 with accuracy around 87 %. The worst case in found for A3-phase, with accuracy close to 80%. We can observe that for all groups specificity is lower than sensitivity by 15%.

B. A-phase Classification

Table III shows the performance of the kNN algorithm among A-phase type separation. The results achieve values higher than 85 % for sensitivity and accuracy while the specificity is slightly lower than 75%. Additionally, Table IV shows the confusion matrix for A-phase type separation. This matrix allows observing how the errors are distributed at the different classes. While A1-phase is well classified by the algorithm, with a percentage close to 90 %,. The worst scenario is obtained for A2-phase, since 46 % of the A2-phases annotated by the expert are classified as A1-phase by the algorithm. Finally, 15 % of A3-phases are misclassified as A2-phase.

TABLE I. SEPARATION BETWEEN BACKGROUND AND A-PHASE DURING ONSET

kNN(k,#features)	Performance (mean +/- sd)		
	Sensitivity (%)	Specificity (%)	Accuracy (%)
A₁ - kNN(11,5)	95 +/- 0.85	90 +/- 1.71	94 +/- 1.14
A₂ - kNN(11,5)	95 +/- 1.13	90 +/- 2.27	93 +/- 1.51
A₃ - kNN(11,5)	92 +/- 1.85	84 +/- 3.69	89 +/- 2.46
A₄ - kNN(11,5)	90 +/- 2.23	80 +/- 4.45	87 +/- 2.97

TABLE II. SEPARATION BETWEEN BACKGROUND AND A-PHASE DURING OFFSET

kNN(k,#features)	Performance (mean +/- sd)		
	Sensitivity (%)	Specificity (%)	Accuracy (%)
A₁ - kNN(13,5)	90 +/- 2.52	81 +/- 5.05	87 +/- 3.37
A₂ - kNN(13,5)	88 +/- 2.70	76 +/- 5.40	84 +/- 3.60
A₃ - kNN(13,5)	85 +/- 2.04	71 +/- 4.08	80 +/- 2.72
A₄ - kNN(13,5)	86 +/- 3.83	73 +/- 7.65	82 +/- 5.10

TABLE III. SEPARATION AMONG A-PHASE TYPE

	Performance (mean)		
	Sensitivity (%)	Specificity (%)	Accuracy (%)
kNN	87.12	74.24	82.23

TABLE IV. CONFUSION MATRIX FOR A-PHASE TYPE

	Expert vs Automatic (%)		
	A1	A2	A3
A1	89.64	9.78	0.58
A2	46.07	42.70	11.24
A3	4.37	15.78	79.85

IV. DISCUSSION

An analysis of the separation between Onset-Offset of A-phases and basal oscillation of the sleep stages, as well as the separation among A-phases types during sleep was presented. The separation assessment is based on the kNN algorithm using as features statistical, complexity, and spectral measures. Our main observations are: a) The separability between the basal sleep stages oscillations and Onset-Offset A-phase, based on a binary classifier, is similar to the inter-scorer agreement, b) A2-phases present characteristics similar to A1-phases, thus they can be easily confounded.

Inter-scorer agreement in locating the A-phases is around 75% [3]. This suggests a 25% of uncertainty in the information observed from the EEG signal to identify the A-phase events. In our analysis, we obtain 80 % of separability between Onset-Offset of the A-phases and the basal sleep stages oscillation. This suggests that features obtained from the EEG signal do not allow a full separation or identification of the A-phases, but the results are close to the human perception. Clearly, it will be interesting to repeat this test with two or more scorers, and evaluate whether the intersection of two scorers is in agreement with the Onset-Offset A-phases that we can correctly separate, this may suggest, the 100 % of the separation could be found by the presented methodology. This would confirm that exist 25 % of subjectivity and uncertainty in the perception of the A-phase activations. In this way, we could define a mathematical model that could give a practical and computational definition of A-phase.

From Table I and II, we can appreciate that Offset separation is a complex task. There exists lower performance and a higher variance in all cases as compared to the Onset case. Those results are expected, since the transition from the A-phase to the basal activity during the Offset is relatively slow and smooth, in contrast to the abrupt amplitude and frequency changes that can be observed during the A-phase Onset.

On the other hand, A-phases types are mainly defined in terms of the frequency content and amplitude of the EEG

signal with respect to the basal EEG oscillations that are present during a specific sleep stage. As can be appreciated from Table IV, A3-phases seem to be well defined and could be classified with acceptable accuracy. However, A2-phases present characteristics or features similar to A1-phases, since a large percentage (> 40 %) of A2-phases are incorrectly classified as A1-phases. This suggests that a deep study is required to understand how to quantify other features that the experts observe, which may not be explicitly defined in the guidelines. On the other hand, while it is possible to apply dimensionality reduction techniques, such as PCA or LDA, to improve the classifier's accuracy, we have decided to focus in a set of features with direct interpretation from a physiological point of view, which may yield useful information about the human perception.

Finally, this study presents some limitations. The number of subjects is small and it is necessary to increase the population to obtain results with a higher confidence. The CAP scoring used in the study was performed by a single scorer. It could be useful obtain the scoring from other experts. Simple classifiers such as linear or quadratic discriminants could be more suitable for this study, since they typically provide more general models which may also yield insight about the neurological mechanisms behind CAP sleep.

V. CONCLUSION

Sleep A-phase Onset seems to be the key for separating the basal sleep stage oscillations from the A-phases, while the A-phase Offset detection resulted to be a more difficult task. To alleviate this problem, a mathematical model of the A-phase decay could be useful to reduce the uncertainty and improve the transition state detection. In addition, A2-phase characteristics presented a large overlapping with A1-phases. For this reason, the kNN classifier was unable to consistently discriminate between both types. Thus, it is a necessary next step to include new features with discriminatory power to improve the results.

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