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Characterization of A phases during the Cyclic Alternating Pattern of sleep

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HIGHLIGHTS

- A quantitative mathematical characterization of sleep microstructure.
- A study that puts the bases for the implementation of an automatic classifier of the Cyclic Alternating Pattern.
- A novel approach to sleep analysis that gives a mathematical confirmation to the medical literature about CAP.

ABSTRACT

Objective: This study aims to identify, starting from a single EEG trace, quantitative distinctive features characterizing the A phases of the Cyclic Alternating Pattern (CAP).
Methods: The C3-A2 or C4-A1 EEG leads of the night recording of eight healthy adult subjects were used for this analysis. CAP was scored by an expert and the portions relative to NREM were selected. Nine descriptors were computed: *band descriptors* (low delta, high delta, theta, alpha, sigma and beta); *Hjorth activity in the low delta and high delta bands; differential variance of the EEG signal*. The information content of each descriptor in recognizing the A phases was evaluated through the computation of the ROC curves and the statistics sensitivity, specificity and accuracy.
Results: The ROC curves show that all the descriptors have a certain significance in characterizing A phases. The average accuracy obtained by thresholding the descriptors ranges from 59.89 (sigma descriptor) to 72.44 (differential EEG variance).
Conclusions: The results show that it is possible to attribute a significant quantitative value to the information content of the descriptors.
Significance: This study gives a mathematical confirm to the features of CAP generally described qualitatively, and puts the bases for the creation of automatic detection methods.

1. Introduction

The electroencephalogram (EEG) provides important and unique information about the sleeping brain. The conventional approach for sleep studies is based on the definition of the sleep *macrostructure*, a stepwise profile that classifies sleep stages according to the prevalent EEG activity in consecutive 30 s epochs. More recent studies have been introduced in sleep research based on the nature and quantitation of the sleep *microstructure*, taking into account the time structure of phasic EEG events observed during non-REM (NREM) stage and shorter than the standardized scoring epoch.

The detection of these events is a fundamental tool for the identification of the Cyclic Alternating Pattern (CAP), which is characterized by sequences of transient EEG variations (phase A) breaking away from the background rhythm of the ongoing sleep stage. Each phase A is characterized by an abrupt frequency/amplitude shift, which coincides with a higher level of brain activation and recurs at intervals up to 1 min long. The intermittent recovery of background activity identifies the interval (phase B) that separates the phases A and corresponds to a lower level of activation. Both A and B phases can last between 2 and 60 s. A CAP cycle is composed of a phase A, and the following phase B. At least two

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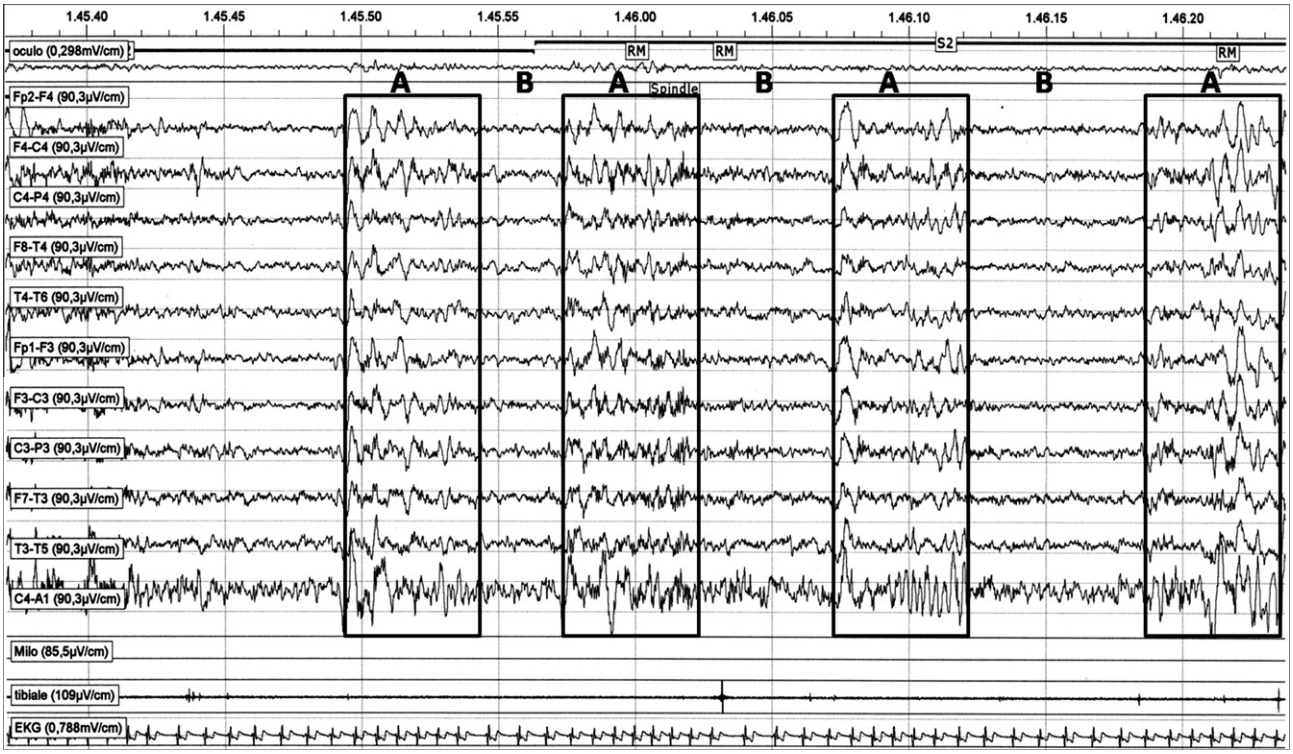

Fig. 1. An example of CAP sequence in sleep stage 2. The boxes outline the phases A of CAP. The EOG, 11 EEG leads, the EMG and the EKG are shown in the screenshot.

consecutive CAP cycles are needed to define a CAP sequence, as shown in Fig. 1. The remaining NREM sleep not occupied by CAP sequences is scored as non-CAP (NCAP).

In relation to the EEG features that compose the phase A of CAP, spectral contents allow classification of three subtypes: (a) A1, dominated by high-voltage delta waves (0.5–4 Hz); (b) A2, when rapid activities occur for 20–50% of the total activation time; (c) A3, characterized by rapid activities, especially beta (15–30 Hz), that occupy more than the 50% of the total phase A duration (Terzano and Parrino, 2000).

In the dynamic organization of sleep, CAP expresses a condition of instability of the level of vigilance that translates the brain effort to preserve and regulate sleep macrostructure. In particular, subtypes A1 are mostly involved in the build-up and consolidation of slow-wave sleep, while subtypes A2 and A3 are closely related and modulate the onset of REM sleep (Terzano et al., 2005).

Specific alterations of phase A subtypes have been described in a number of sleep disorders such as nocturnal frontal lobe epilepsy (Zucconi et al., 2000), sleep apnea (Terzano et al., 1996), insomnia (Terzano et al., 2003; Parrino et al., 2004) and narcolepsy (Terzano et al., 2006).

At the present time, analysis of CAP parameters is performed only through visual methods by identifying EEG events such as delta bursts, vertex sharp transients, K-complex sequences with or without spindles, polyphasic bursts, K-alpha, intermittent alpha, EEG arousals, which constitute the basic phase A features for CAP scoring (Terzano et al., 2001).

In spite of the consolidated relevance of the visual methodology, still the gold standard for scoring sleep, the quantitative assessment of sleep measures is a time-consuming procedure. Moreover, visual analysis can be biased by a certain degree of inter-scorer agreement, ranging from 69% to 77% (Rosa et al., 2006). In order to overcome these issues, the research of quantitative measures of the EEG, capable of distinguishing CAP A phases from the background, is desirable with the final purpose of achieving an automatic detection algorithm. So far, only a few studies have presented methods for the automatic analysis of CAP (Rosa et al., 1999; Navona et al., 2002; Barcaro et al., 2004; De Carli et al., 2004; Largo et al., 2005; Ferri et al., 2005).

In all these methods, the computation of "short–long term ratios", performed in combination with other methods of analysis and often connected to a model for the sleep EEG generation, has allowed the achievement of interesting results. However, a robust universal method for the detection of CAP is still missing and nowadays it is not easy to introduce CAP studies in everyday clinics with appropriate confidence and fast scoring.

The aim of this work is to exploit the results of previous studies, integrated by an analytical evaluation of the information content of each descriptor and introducing new descriptors that could improve the automatic recognition of CAP A phases.

2. Methods

The data analyzed in this study were extracted from all-night PSG recordings collected at the Parma Sleep Disorders Centre database. Eight normal subjects, four males and four females, aged between 23 and 35 years (23-year-old subjects, one 24, two 30-year-old, one 31, one 32 and one 35), were selected after the accomplishment of an entrance investigation. Subjects were evaluated in order to obtain a homogeneous group and were free from psychiatric, neurological and medical disorders. Sleep/wake schedule was investigated for 14 days before the PSG recordings with a sleep log. Inclusive criteria were the absence of sleep disorders and daytime napping. A personal interview integrated by a structured questionnaire confirmed good vigilance level during daytime, normal sleep habits without any difficulties in falling or remaining asleep at night. All participants were requested to refrain from any drug intake and excessive alcohol or coffee consumption in the previous 3 weeks preceding the PSG recording. All subjects slept at least two consecutive nights in a video-monitored, temperature-controlled and sound-proof (Leq < 35 dB) laboratory. The first night was used for adaptation to the recording