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A general automatic method for the analysis of NREM sleep microstructure

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Abstract

Objective: To define a unified method for the automatic recognition and quantitative description of EEG phasic events of sleep microstructure occurring during NREM sleep, particularly arousals, phase A subtypes of cyclic alternating pattern and spindles.

Methods: The NREM sleep EEG of 10 normal young subjects was examined in order to recognize formal phasic events of sleep microstructure. The following 'formal' events (i.e. events defined exclusively on the basis of automatic analysis criteria) were classified: arousals, A1-phases (A-phases not including arousals) and A2- and A3-phases (A-phases including arousals). Spindle bursts, corresponding to visually recognized spindles, were also formally defined. The identification of these events was carried out following a three-step procedure: (1) computation of band-related descriptors derived from the EEG signal, (2) introduction of suitable thresholds and (3) application of simple logical principles, i.e. an exclusion principle and an overlapping principle.

Results: Formal A-phases, arousals and spindle bursts showed spectral characteristics which were consistent with visual inspection. The value of the parameter Correctness for the recognition of the A-phases was 83.5%. In particular, the different physiological distribution of the A-phases in Stage 2 preceding slow wave sleep with respect to Stage 2 preceding REM sleep was confirmed.

Conclusions: The proposed method provides a unified quantitative approach to the study of sleep microstructure. Visually defined events can be reliably identified by means of automatic recognition.

Keywords: Automatic EEG analysis; Sleep microstructure; Cyclic alternating pattern; Arousals

1. Introduction

1.1. The twofold role of transient events in sleep scoring

Transient EEG waveforms or, more generally, transient polygraphic events play a twofold role in sleep analysis.

First, their occurrence and their rate of occurrence are fundamental in visual scoring of polysomnographic measures according to Rechtschaffen and Kales' [1] rules. Events such as K-complexes, alpha bursts, spindles and vertex sharp waves are well-known markers for stage scoring.

Many transient events are not only landmarks for sleep stage recognition but their occurrence plays an active role in the dynamics of the sleep profile. This consideration is supported by the increasing interest in arousals and other microstructure components of sleep. The term microstructure refers to EEG features below the time dimension of the conventional 20–30 s scoring epoch [1]. The recognition of microstructure events provides physiological and clinical information which integrates the macrostructure measures obtained with the conventional staging system.

The criteria for recognition and classification of arousals were established in 1992 by the American Sleep Disorders

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Association [2]. Agreement was found on the following definition: 'An EEG arousal is an abrupt shift in EEG frequency, which may include theta, alpha and/or frequencies greater than 13 Hz, but not spindles. The EEG frequency shift must be 3 s or greater in duration to be scored as an arousal.'

Another significant microstructure phenomenon is cyclic alternating pattern (CAP) [3]. Criteria for the recognition and classification of CAP were given in 2001 in a Consensus Report [4], defined as the following: 'The CAP is a periodic EEG activity of non-REM sleep. CAP is characterized by sequences of transient electrocortical events that are distinct from background EEG activity and recur at up to 1 min intervals.' Recurring electrocortical events are called A-phases and are divided into three classes: A1, A2, and A3. CAP appears spontaneously but also in association with identifiable sleep pathophysiologies such as sleep disordered breathing [5] and periodic limb movement disorder [6]. CAP evaluation includes the periodicity dimension in the arousal process and attributes different levels of cerebral activation as expressed by the phase A subtypes.

The phase A1 subtypes are composed of K-complexes and delta bursts; they prevail in Stage 2 that precedes slow wave sleep. Phases A2 and A3 of CAP are composed of mixed EEG patterns including both slow and rapid activities; they prevail in Stage 2 that precedes REM sleep. An extensive overlap between ASDA arousals and subtypes A2 and A3 has been demonstrated [7]. Due to their complex EEG morphologies, arousals and CAP include a variety of transient changes in different frequency bands.

1.2. Automatic analysis of microstructure phenomena

A number of automatic and quantitative methods for the analysis of microstructure phenomena have been carried out in the last decades. These methods often present high agreement with visual analysis. We limit ourselves to reporting briefly some of the most interesting events. A general model for the analysis of sleep spindles and alpha rhythms was proposed in the 1980s [8,9]. It was based on the idea that EEG phenomena are generated by excitatory and inhibitory neuronal populations interacting by means of feedback loops. This model was then also applied to the detection of vertex waves and K complexes [10]. In 1994, Jobert et al. [11] suggested the application of the Wavelet Transform to the analysis of transient events and supported this idea with preliminary significant results. Pardey et al. [12] proposed a neural network EEG analysis system based on an autoregressive modeling of the signal; the EEG was quantified on a continuous scale which was not linearly related to conventional sleep stages. McKeown et al. [13] described a method for detecting stage changes in the EEG, which was based on the properties of a dimensionless function calculated by using independent component analysis. De Carli et al. [14] detected arousals applying the Wavelet Transform to two bipolar EEG traces and one EMG derivation. In a following study the same group [15] compared the mean power values of the entire arousal with the immediately preceding 3.5 s and found an enhancement in the band of delta power relative to background. An automatic system for the detection of CAP sequences was proposed by Rosa et al. [16]. The system consisted of three parts: a model-based maximum likelihood estimator, a variable length template-matched filter, and a state machine rule-based decision subsystem. The Matching Pursuit Procedure, based on the decomposition of the signal into waveforms with good localization in time and frequency, was applied to the identification and parameterization of spindles [17,18]. The method for spindle detection described by Huupponen et al. [19] was based on the application of a variable threshold the value of which was estimated by Bayesian analysis. More recently, Huupponen et al. [20] identified, via a mean frequency measure and FFT, sleep oscillations with period times of 50–150 s having a relatively large amplitude.

1.3. Approaches to automatic analysis

There are two different approaches for assessment of automatic analysis of sleep EEG. One is the agreement with the output of visual analysis. A remarkable example is provided by the so-called 'hybrid' systems, developed in the 1970s, which are in part analog and in part digital. These systems achieve a high rate of agreement with visual scoring [21,22]. A second approach is based on the idea that automatic signal processing can provide additional information with respect to that given by visual analysis. An example can be given by the characteristic damped-oscillation pattern of the delta rhythm [23–25], which provides important information, the details of which are not contained in the histogram.

According to Kubicki et al. [26], an automatic analysis of sleep EEG should emphasize the strengths of the computer, with a substantial independence from visual analysis. The Rechtschaffen and Kales' rules [1] are conventional criteria but can be inadequate for computer-based automatic analysis.

If these considerations can be applied to the analysis of sleep profile, they are even more suitable for the analysis of phasic events of sleep microstructure. The aim of the study was to define a unified method that stems from the characteristics of visual analysis and introduces new criteria closely connected to the discriminating properties of automatic analysis.

2. Methods

2.1. General properties of the approach

The method applied in this study is an extension of the computer-based procedure previously used for the recognition of CAP A-phases [27,28]. A-phases including no arousals and with dominant EEG slow patterns are assigned to A1 subtypes; this pattern is identified when the delta descriptor crosses a given threshold even for a very short time. The assignment of an A-phase to subtypes A2 or A3 is based on the recognition of an arousal within the A-phase [4]; the occurrence of this arousal is recognized by the crossing of a given threshold by at least one of the theta, alpha or beta descriptors.

We based the analysis of microstructure events on the identification of two fundamental patterns (A-phases with slow EEG components and arousals), and on their temporal overlap. Because the adopted definitions partially bypass visual criteria, automatically recognized events were defined as 'formal'.

2.2. Subjects and devices

The sleep EEG of 10 young subjects (5 males and 5 females) was studied. They presented no primary medical or psychiatric disorder and used no drugs affecting the central nervous system. Age ranged from 22 to 29 years. The analysis was carried out on the third of three consecutive nights spent in the sleep laboratory. The polygraphic recording included eight EEG derivations (F3-C3, C3-P3, P3-O1, F4-C4, C4-P4, P4-O2, C3-A2 and C4-A1), EOG, EMG and respiration. The Galileo System (Esaote Biomedica) was used for signal acquisition, filtering and recording. Sleep stages were visually scored. A visual recognition of the principal microstructure events was also carried out.

2.3. EEG signal processing

The F4-C4 signal was used for automatic analysis. It was filtered between 0.5 and 25 Hz (filter slope: 24 dB/oct), sampled at 128 Hz and recorded on a CD.

The analysis procedures were written in Visual Basic 6 and run on a PC.

Using an FFT algorithm over intervals lasting 64 s, the F4-C4 trace was decomposed into five band components: delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), sigma (12.5–14.5 Hz) and beta (15–20 Hz). For the computation of the components, rectangular filters in the frequency domain were applied and then the inverse Fourier transforms were computed. All the remaining analyses were performed in the time domain.

For each component, two amplitude averages were computed every 0.5 s: one over an interval lasting 2 s and the other over an interval lasting 64 s. The difference between these two amplitudes, divided by the amplitude of the average over the longer epoch, gave the dimensionless band descriptor in the instant considered (the center of both intervals). Amplitude was simply defined as the absolute value of the signal. The time lengths for the averages were chosen for following reasons:

(a) the longer length was consistent with the time lengths usually considered for the construction of the hypnogram;
(b) the shorter length was taken according to two opposite needs: it had to be short to provide information about 'instantaneous' events and long enough to cover an entire period of the slowest Fourier component considered (0.5 Hz); this length has been applied often in the automatic analysis of microstructure events [29].

Two thresholds were introduced: the existence threshold, equal to one, and the length threshold, equal to zero. Two conditions were applied to recognize and classify the epochs characterized by a microstructure event: (1) for at least one instant, the existence threshold was overcome; (2) for all instants (apart from isolated ones), the length threshold was overcome. In other words, given a recognized event, the existence threshold was overcome at least once by the relevant descriptor (or by one of the relevant descriptors) and the limits of the event were given by the first two consecutive points at the left and the first two consecutive points at the right, characterized by values of the relevant descriptor (or all relevant descriptors) below the length threshold. The relevant descriptors were those indicated in the definitions of the various formal events (see Section 2.4).

For arousals, an 'exclusion condition' assured that the delta band was not involved. The application of the exclusion condition implied the introduction of a third threshold.

An 'overlapping principle' was also applied to recognize: (a) sub-events occurring during a different event (e.g. an arousal inside an A-phase) or (b) different events occurring one immediately after the other (for instance two A-phases separated by less than 1.5 s, which were unified into a single A-phase; the value 1.5 s was chosen according to the visual criteria for intervals between A-phases).

In order to see the interesting cases in which the slower components in the delta band behaved differently from the faster components in the same band, two additional descriptors were computed for the lower delta (0.5–2 Hz) and the higher delta (2–4 Hz) bands.

2.4. Definitions of the considered events

The following list reports the events considered for the study of NREM sleep microstructure and their definitions according to the automatic procedure.

1. Formal arousals:
   - Existence threshold applied to theta, alpha and beta bands.
   - Length threshold applied to theta, alpha and beta bands.
   - Exclusion principle applied to delta band.
   - Constraint due to the overlapping principle: no overlapping with formal A1-phases.

  – Subtypes: (1) theta arousals; (2) alpha arousals; (3) beta arousals. (When two descriptors overcame the existence threshold, the arousal was labeled according to the band characterized by higher values of the descriptor.)
2. Formal A1-phases:
  – Existence threshold applied to delta band.
  – Length threshold applied to theta, alpha, sigma and beta bands.
  – Exclusion principle: none.
  – Constraint due to the overlapping principle: no overlapping with formal arousals.
  – Subtypes: none.
3. Formal A-phases with arousals:
  – Existence threshold applied to delta band.
  – Length threshold applied to theta, alpha, sigma and beta bands.
  – Exclusion principle: none.
  – Constraint due to the overlapping principle: overlapping with formal arousals. (The application of this overlapping principle obviously implied the indirect application of different criteria for the thresholds and for the exclusion principle.)
  – Subtypes: (1) theta A-phases; (2) alpha A-phases; (3) beta A-phases.

Formal spindle bursts, corresponding to visually recognized spindles, were also considered in order to check the applicability of the method to transient events different from CAP A-phases and arousals. We limited ourselves to events lasting at least 2.5 s. We checked, however, that a selective decrease of the shorter average epoch for the sigma component made it possible to recognize shorter spindles. Formal spindle bursts were defined as follows:

– Existence threshold applied to sigma band.
– Length threshold (2.5 s) applied to sigma band.
– Exclusion principle: none.
– Overlapping principle: see ‘Subtypes’.
– Subtypes: (1) inside a formal A1-phase; (2) outside any formal A1-phase.

For simplicity’s sake we defined the formal events in the same way for all the NREM stages. For the same reason we did not include duration limits in the formal definitions. However, only formal A-phases lasting at least 2 s and formal arousals lasting at least 3 s were considered for the statistical comparisons with visually recognized events.

2.5. Statistical analyses of the results

First, a statistical analysis was made to check that formal events met the same fundamental properties of the correspondent visual events. These properties are well-known. For instance, arousals are much less numerous during Stage 4 than during Stage 2. The data set for the statistical analysis consisted of the frequencies (number of events per minute) of the various events for each subject and for each NREM stage. The mean values in the different stages were compared, applying the non parametric one-tailed Wilcoxon’s *t*-test and requiring $P<0.01$ as the statistical significance level.

An interesting result provided by the visual analysis of CAP has been a different distribution of the ratio of the A1-phases to all the A-phases in Stage-2 epochs preceding Stage 3 with respect to Stage-2 epochs preceding REM sleep. In order to verify whether this result was also valid for formal events, the frequencies of formal A1-phases and of formal A-phases with arousals were calculated over the last 10 min of Stage 2 preceding Stage 3 and over the last 10 min of Stage 2 preceding REM sleep in the first sleep cycle for each subject. A one-tailed Wilcoxon’s *t*-test was applied to the values so obtained; a significance level $P<0.01$ was required.

A second statistical analysis was carried out to measure the agreement between the formal events and the corresponding visual events. A 4×4 matrix was thus constructed considering two scoring methods, the visual and the automatic, and four possibilities:

1. formal arousals (or visually recognized arousals);
2. formal A1-phases (or the correspondent visually recognized events);
3. formal A-phases with arousals (or the correspondent visually recognized events);
4. no events (according either to automatic criteria or to visual criteria).

Table 1
Number of detected formal events per minute and standard deviations for the 10 subjects during the various NREM sleep stages

	Stage 1 (15.8 ± 2.7 min)	Stage 2 (190.6 ± 18.7 min)	Stage 3 (37.0 ± 7.4 min)	Stage 4 (59.8 ± 6.9 min)
Formal theta arousals	0.17 ± 0.04	0.01 ± 0.01	0.05 ± 0.04	0.01 ± 0.01
Formal alpha arousals	0.48 ± 0.07	0.10 ± 0.02	0.14 ± 0.06	0.02 ± 0.01
Formal beta arousals	0.09 ± 0.06	0.01 ± 0.01	0.02 ± 0.02	0.01 ± 0.01
Formal A1-phases	0.29 ± 0.10	0.92 ± 0.13	0.59 ± 0.17	0.28 ± 0.08
Formal theta A-phases	0.10 ± 0.07	0.22 ± 0.03	0.04 ± 0.04	0.09 ± 0.04
Formal alpha A-phases	0.46 ± 0.04	0.26 ± 0.04	0.15 ± 0.04	0.01 ± 0.01
Formal beta A-phases	0.01 ± 0.01	0.14 ± 0.04	0.04 ± 0.03	0.01 ± 0.01
Formal spindle bursts (lasting at least 2.5 s)	0.61 ± 0.14	1.05 ± 0.19	0.56 ± 0.07	0.43 ± 0.12

Table 2
Comparison of the mean frequency of the different formal events in the various sleep stages

	S1 versus S2	S1 versus S3	S1 versus S4	S2 versus S3	S2 versus S4	S3 versus S4
Formal arousals	More frequent in Stage 1	More frequent in Stage 1	More frequent in Stage 1		More frequent in Stage 2	More frequent in Stage 3
Formal A1-phases	More frequent in Stage 2			More frequent in Stage 2	More frequent in Stage 2	More frequent in Stage 3
Formal A-phases with arousals		More frequent in Stage 1	More frequent in Stage 1	More frequent in Stage 2	More frequent in Stage 2	More frequent in Stage 3

Empty cells indicate no statistical significance. Filled cells indicate statistical significance according to the Wilcoxon's *t*-test with $P<0.01$.

From this 4×4 matrix two parameters were then computed:

- Correctness, given by the ratio of the number of events for which there was agreement (the sum of the diagonal elements), to the total number of events;
- Cohen's kappa, a statistical parameter able to provide a measure of the agreement between different scorers (or different scoring methods), statistically discarding the cases in which the agreement is due to chance. Considering that in Tables 1–4 only recognized events were reported, and all the instants, for which there was agreement between visual and automatic analysis in not recognizing any event, were not considered, even not very high values of kappa should be viewed as corresponding to good levels of agreement.

It was then checked that the significance level of Cohen's kappa with respect to agreement by chance was extremely high; the criterion $P<0.0001$ was applied.

A comparison between different values of the three thresholds was then performed to check that the chosen values were appropriate. This check was simply performed, changing the values of the thresholds one by one. The choice criterion was the agreement between visual and automatic analysis, measured by the parameter Correctness.

3. Results

3.1. Graphical representation of the descriptors

The graphical representation of the descriptors during a recognized microstructure event evidenced the properties of any considered epoch: its length, the frequency bands involved, the level of this involvement, and the possible delays between the peaks of different band descriptors.

Four examples are shown in the figures. The full time scale is the same, 20 s, for all the figures; the recognized epochs, whose beginning and end are indicated by vertical cursors, are completely included in the 20 s intervals. The figures show, respectively:

(1) a formal A1-phase during Stage 4 lasting 14 s, characterized by a different behavior of the slower delta descriptor with respect to the faster delta descriptor (Fig. 1);
(2) a formal A-phase with arousal during Stage 2 lasting 17.5 s, presenting a two-modal behavior of the delta descriptor (Fig. 2);
(3) an arousal during Stage 1 lasting 5.5 s, characterized by amplitude increases in the alpha and beta bands (Fig. 3);
(4) a formal spindle burst during Stage 2 lasting 4 s, preceded by a spindle burst recognized by the automatic method as a separate event (Fig. 4).

Table 3
Comparison of the frequency (number of events per minute) of the two kinds of formal A-phases in Stage 2 preceding REM sleep with respect to Stage 2 preceding slow wave sleep

	Stage 2 before Stage 3	Stage 2 before REM sleep
Formal A1-phases	1.15 ± 0.18	0.91 ± 0.15
Formal A-phases with arousals	0.49 ± 0.11	1.10 ± 0.15

The mean ratio between the two frequencies was significantly different in the two conditions, according to the Wilcoxon's *t*-test with $P<0.01$.

Table 4
The 4×4 agreement matrix for the microstructure events recognized either by visual analysis or by automatic analysis or by both

	Formal arousals	Formal A1-phases	Formal A-phases with arousals	No formal event
ASDA arousals	371	27	23	38
CAP A1-phases	11	1735	182	184
CAP A2- and A3-phases	24	229	981	75
No visual recognition	40	169	98	0 (not considered)

Each cell reports the number of events for which the automatic analysis provided the assignment indicated in the column title and the visual analysis the assignment indicated in the row title. Formal A-phases lasting less than 2 s and formal arousals lasting less than 3 s were not considered. The cases for which there was agreement between the automatic recognition of a formally defined event and the visual recognition of the correspondent visually defined event are those in the diagonal cells. The zero in the last cell indicates that only recognized events were considered.

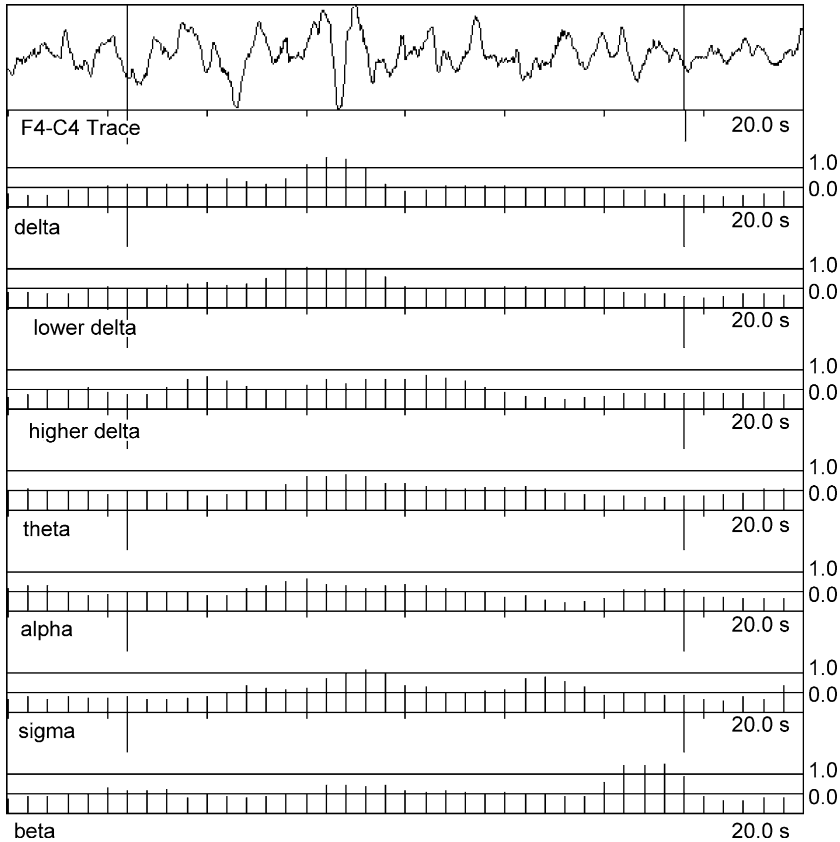

Fig. 1. A formal A1-phase during Stage 4. The top curve represents the F4-C4 trace during a 20 s interval including the A1-phase, the beginning and end of which (as identified by the automatic procedure) are indicated by vertical cursors. The other curves show the descriptors, sampled every 0.5 s, for the following frequency bands (from top to bottom: delta, lower delta, higher delta, theta, alpha, sigma and beta). The two horizontal lines in the descriptor graphs represent the existence threshold and the length threshold, respectively. The time length of the phase, given by the time distance between the two vertical cursors, was 14 s. The individual characteristics of the A1-phase were as follows: gradual increase of the delta descriptor at the beginning, different behavior of the slower delta component with respect to the faster delta component, very short beta amplitude increase toward the end, high values of the sigma descriptor in the middle of the phase.

3.2. Recognition of microstructure events: summary of the results obtained

Table 1 provides the mean values of the number of detected events per minute in the different NREM sleep stages.

Table 2 shows that the mean number of the various detected events per minute generally varied significantly according to the sleep stage. For this analysis, the various formal arousals and formal A-phases with arousals were put together. The statistically significant variations were in agreement with the variations reported in the literature [30] for the corresponding visual events.

The comparison of the distribution of the A-phases in the 10-min Stage 2 preceding Stage 3 and REM sleep, respectively, provided the results indicated in Table 3, which confirmed the differences in the distribution of the different classes of visually recognized A-phases.

3.3. Measure of the agreement between the automatic recognition of formally defined events and the visual recognition of visually defined events

The study of the agreement between automatic and visual recognition was carried on the agreement matrix represented in Table 4.

If we only consider the recognition of the CAP A-phases without taking into account the discrimination between different classes, we obtain from Table 4 the following: cases of agreement: 3127; false positives: 317; and false negatives: 294. The value of Correctness for the A-phases recognition was therefore similar to the agreement percentage between visual scorers. In fact, Correctness $=3127/(3127+317+294)=83.5\%$.

A statistical analysis of Table 4 was then carried out including the assignments to the different classes. The following results were obtained:

Correctness $=3087/4187=73.7\%$; Cohen's kappa $=0.58$; kappa's sigma $=0.02$; $P<0.0001$.

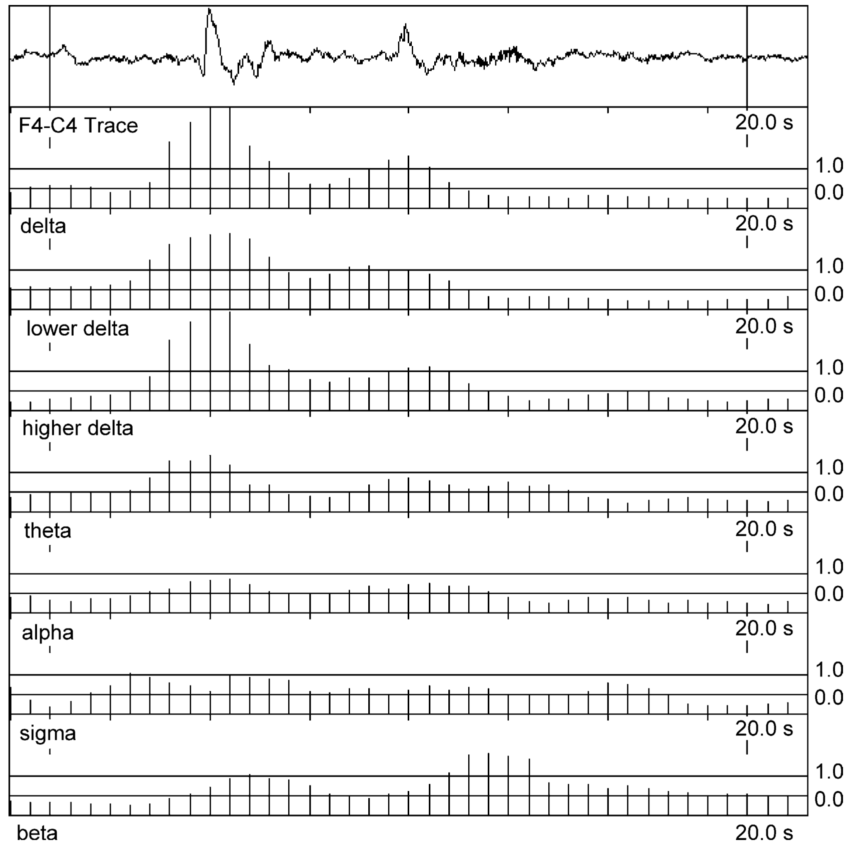

Fig. 2. A formal A-phase with arousal during Stage 2 lasting 17.5 s. The eight curves have the same meaning as in Fig. 1. The individual characteristics of the A-phase were as follows: two-modal behavior of the delta descriptor with a 5 s shift between the peaks; occurrence of a beta arousal whose peak was delayed 2 s with respect to the second delta peak; waveform presenting a remarkable delta component at the beginning.

This level of agreement was close to the agreement between different visual scorers. Moreover, in the 53% of the cases of disagreement between visual and automatic analysis, the visual scorer, when asked to comment on the disagreement, answered that, according to a further reflection based on the criteria for visual analysis, it was better to change the visual assignment.

The value of Correctness for arousals (considering those within an A-phase together with those outside any A-phase) was lower, equal to 69%.

We checked qualitatively that the agreement between the automatic recognition of formal spindle bursts lasting at least 2.5 s and the visual recognition of spindle activity lasting at least 2.5 s was good. A quantitative analysis considering five subjects was carried out. The number of events for which there was agreement was 2185; the number of events recognized only by the automatic procedure was 379, and the number of those recognized only visually was 361. The Correctness was 75%. With regard to shorter spindle activity, we limited ourselves to check qualitatively that a reduction from 2.0 to 0.5 s of the interval for the amplitude average implied a fairly high level of agreement in the recognition of spindles of any time length.

4. Discussion and conclusion

The method described provides a general unified automatic and quantitative approach to the study of sleep microstructure. It is characterized by extreme simplicity under various aspects. A single EEG trace was processed; we chose the F4-C4 trace, but similar results could be obtained analyzing the other traces. Two basic patterns, arousals and CAP phase A subtypes, were included in the definition of formal events. The ranges of the various frequency bands were very similar to those implied in the visual analysis of the EEG traces. The definitions of the descriptors were mathematically elementary. The threshold levels were given by round numbers (0 and 1) for the length threshold and the existence threshold, respectively; it was necessary, however, to introduce a third threshold, in order to apply the exclusion principle. This threshold was equal to 0.75.

Although we found that the application of the method to other traces altered the results very slightly, we feel that it will be very important to study the topographical changes and their meaning. It is interesting to observe that preliminary results obtained applying this method to the recognition of transient events during REM sleep show that,

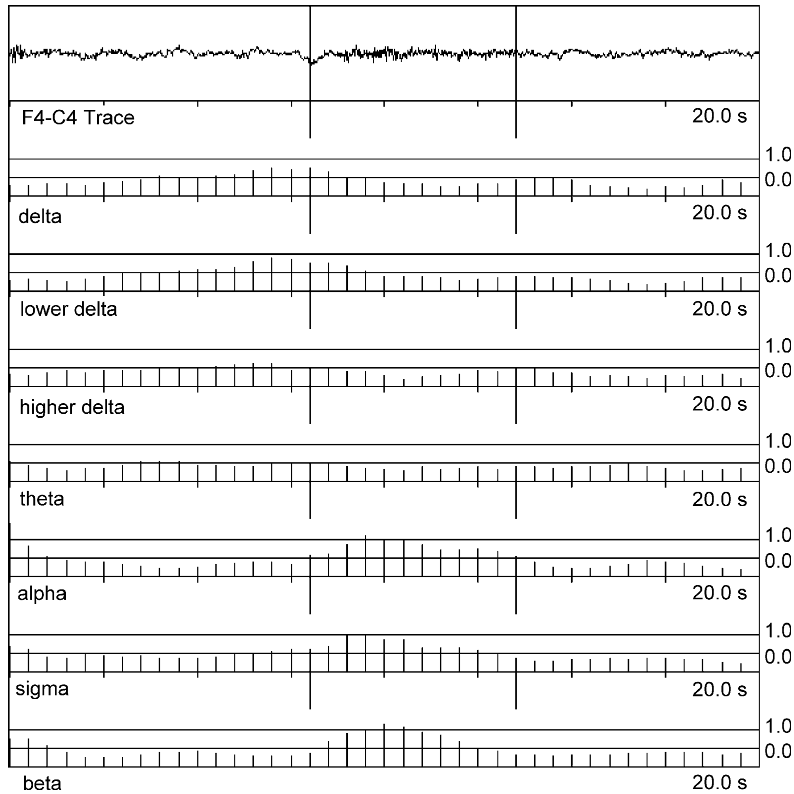

Fig. 3. An arousal during Stage 1 lasting 5.5 s characterized by amplitude increases in the alpha and beta bands. The eight curves have the same meaning as in the preceding figures. The alpha and beta descriptors increased almost simultaneously, while the decrease occurred earlier for the beta descriptor.

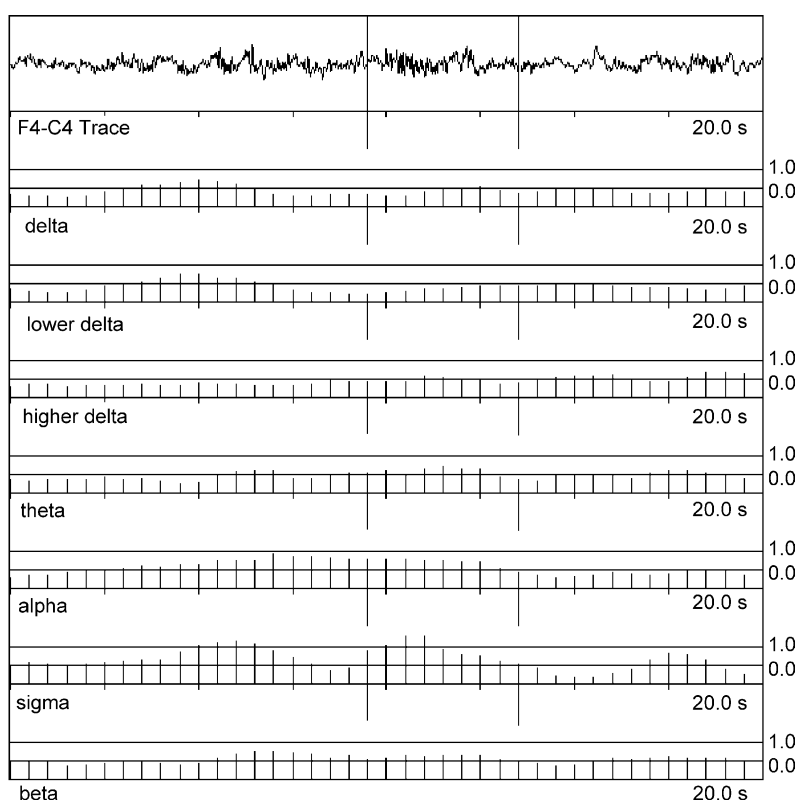

Fig. 4. A formal spindle burst during Stage 2 lasting 4 s. The eight curves have the same meaning as in the preceding figures. This spindle burst was preceded by another spindle burst which was separately recognized by the automatic method. For both events, no descriptor other than the sigma descriptor overcame the existence threshold.

unlike NREM sleep, there are fairly numerous events the recognition of which depends on the trace analyzed.

The visual impact of the descriptors in the time domain was an important issue. After an initial application of the Fourier Transform in order to separate the various frequency components of the signal, the whole analysis was carried out in the time domain.

In most of the cases of discrepancy between automatic and visual analysis, both the following facts occurred: (a) the visual operator was not sure of his choice; (b) values of the descriptors not far from the thresholds were determinant for the result provided by the automatic method. In other words, the uncertainty was indicated in the data, much more than in the visual or automatic procedure. This uncertainty, which often concerned the discrimination between the A1-phases and the A2-phases, accounts for the lower value found for Correctness if only arousals are considered.

Future research should improve the methods in three directions: in increasing the conceptual explicative power of the model, in increasing the agreement with visual analysis, and in increasing the range of applications. We feel that a full exploitation of the flexibility of the method could improve it. For instance, a selective reduction of the average interval for the higher frequency bands can lead to the recognition of very short transients.

In conclusion, the rules for macrostructure analysis are pointed out in the Rechtschaffen and Kales' system, which is, however, based on giving a single definition (stage) to a relatively large homogeneous epoch of 20 or 30 s. In contrast, the microstructure events are complex, stand against a tonic background, last a few seconds and still present several changing patterns. In the lapse of a few seconds, EEG features may shift rapidly from slow, high-voltage waves to fast, low-amplitude rhythms involving completely different cerebral areas and biochemical pathways. This can be skipped or difficult to follow-up only by eye inspection. Naturally, automatic detection should be in tune with the visual data. However, once the rules for visual analysis of microstructure have been established [31,32], the time is ripe to exploit all the available automatic analysis systems to gain insight into the knowledge of sleep regulation which cannot be defined by visual detection. The methodology proposed in this paper can be a new simple tool for the achievement of innovative information.

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