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Consensus Report

Atlas, rules, and recording techniques for the scoring of cyclic alternating pattern (CAP) in human sleep

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1. Definition of cyclic alternating pattern

The cyclic alternating pattern (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.

2. Background and overview

The CAP is an EEG activity that may signify sleep instability, sleep disturbance, or both. CAP can appear spontaneously in non-REM sleep, but it can occur also in association with identifiable sleep pathophysiologies (e.g. sleep-disordered breathing and periodic leg movement activity). Individual variants of CAP have been recognized and are well described, albeit known by other names (for example, periodic K-alpha). The CAP sequence, originally conceptualized as an arousal phenomenon, has evolved theoretically to encompass both the process of sleep maintenance and sleep fragmentation. With respect to CAP as an arousal process, its subtype classification extends the current American Sleep Disorders Association definitions to include a periodicity dimension and a possible marker of pre-arousal activation.

High-amplitude EEG bursts, be they delta-like or K-complexes, have long been thought to reflect a possible arousal process. However, evidence connecting such phenomena to clinical correlates typical of sleep disturbance was lacking. An alternative view is that these phenomena are associated with sleep instability (possibly an external or internal challenge to the sleep process) and that this type of slow wave activity (subtypes A1 of CAP) marks the brain's attempt to preserve sleep. However, if sleep becomes too unstable or the preservation attempt fails, then a frank EEG arousal will accompany or replace the high-amplitude, slow activity. Thus, subtypes A2 and A3 of CAP constitute a central nervous system arousal.

This atlas and standardized manual are designed to facilitate utility of CAP recording and scoring and to provide a consensus terminology. The committee hopes that the system will be useful and will help stimulate investigation in this area of sleep research. For example, cyclic autonomic activations' potential linkage with the sleep process, the role of increasing and decreasing synchronization, and the failure to maintain sleep continuity in some pathological conditions can be explored using CAP analysis. Additionally, factors that alter CAP periodicity may provide a clue to the overall sleep process. It is hoped that the addition of a periodicity dimension to the concept of sleep stability and arousal will provide a new and valuable perspective to

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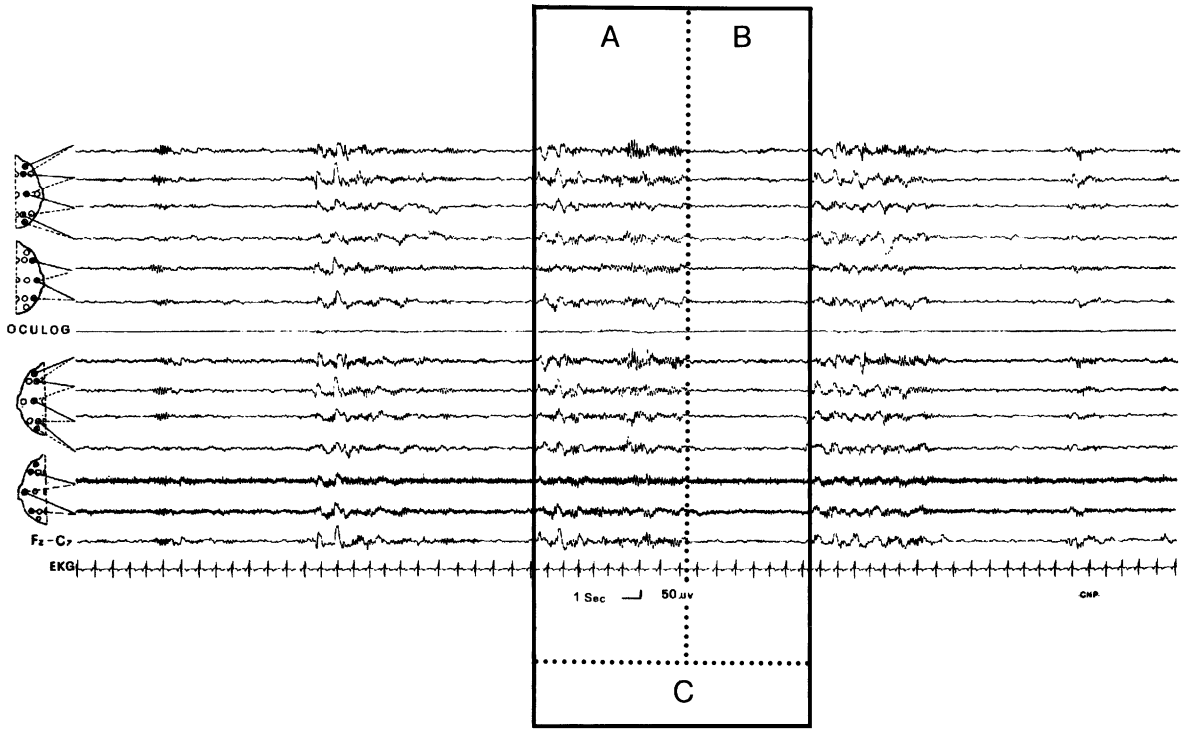

Fig. 1. An example of cyclic alternating pattern (CAP) in sleep stage 2. The box outlines a CAP cycle (C) composed of a phase A (A) and the following phase B (B). Bioplolar EEG derivations using international electrode placement; top 6 channels from top to bottom: FP_2–F_4, F_4–C_4, C_4–P_4, P_4–O_2, F_8–T_4, T_4–T_6; bottom 7 channels from top to bottom: FP_1–F_3, F_3–C_3, C_3–P_3, P_3–O_1, F_7–T_3, T_3–T_5, F_z–C_z; OCULOG: Oculogram; EKG: Electrocardiogram.

appreciate underlying physiological sleep mechanisms. CAP analysis is not meant to replace sleep stage scoring or arousal scoring, but rather to extend quantitative sleep analysis and provide a new tool to use in our quest to understand human sleep.

3. Rhythms

Rhythms (delta, theta, alpha, beta, spindles) are uninterrupted, tonic bioelectrical cerebral oscillations. Subdivided into frequency bandwidths, they constitute the EEG background and vary according to overall neurophysiological state; that is, wakefulness, non-REM sleep, and REM sleep.

Rhythms may be interrupted by periodic EEG activities.

4. Periodic EEG activities

Periodic EEG activities are electrocortical events recurring at regular intervals in the range of seconds. These EEG features are clearly distinguishable from the background rhythm as abrupt frequency shifts or amplitude changes.

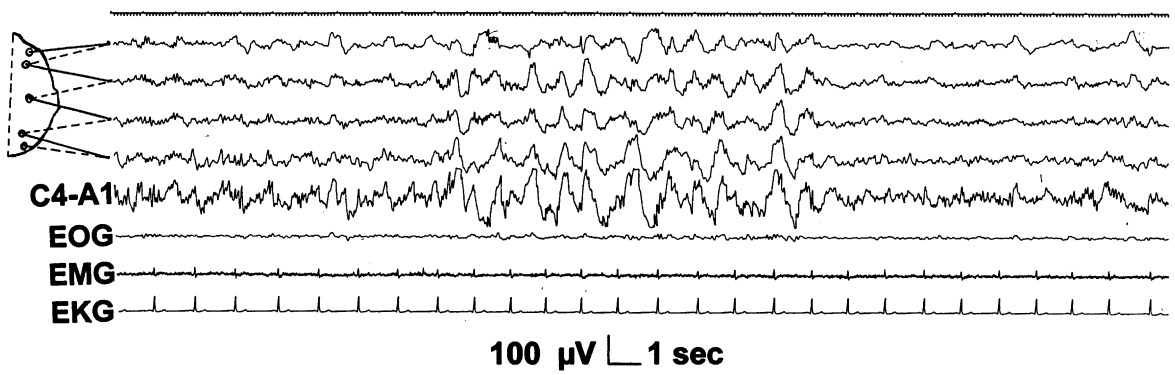

Fig. 2. Delta burst in slow wave sleep. Top 4 channels: Bioplolar parasagittal EEG derivation of the right side similar to top 4 channels in Fig. 1; C4–A1: C4 connects to left ear (A1); EOG: Electrooculogram; EMG: Electromyogram; EKG: Electrocardiogram.

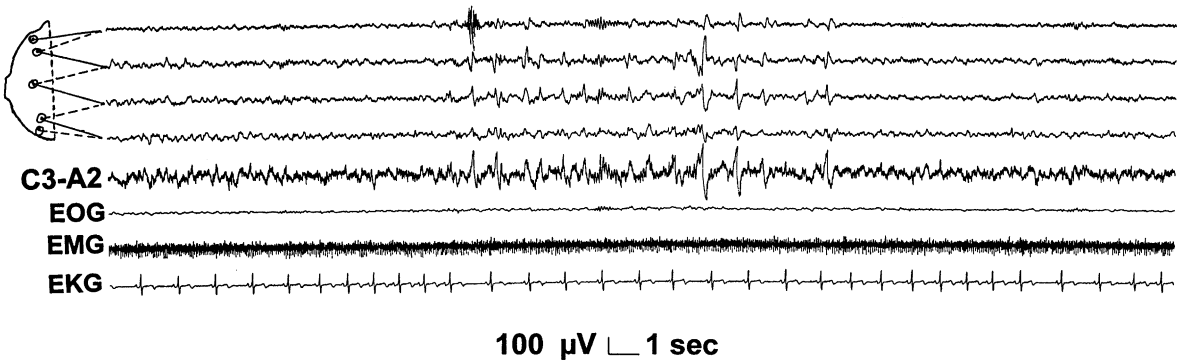

Fig. 3. Sequence of vertex sharp transients during the transition from stage 1 to stage 2 sleep. Top 4 channels: Bipolar parasagittal EEG derivation on the left side similar to channels 8, 9, 10, 11 from Fig. 1; C3–A2: C3 connected to right ear (A2).

Periodic activities can be characterized with three parameters:

1. The repetitive element (phase A of the period), represented by the recurring EEG feature.
2. The intervening background (phase B of the period), identified by the interval that separates the repetitive elements.
3. The period or cycle (the sum of phase A and phase B duration), characterizing the recurrence rate.

5. Cyclic activities or cyclic alternating pattern

CAP is a specific type of periodic activity in which both phase A and phase B can range between 2 and 60 s. A phase A (A) and the following phase B (B) compose a cycle (C) (Fig. 1).

CAP appears throughout sleep stages 1, 2, 3, 4.

Phase A of CAP is identified by transient events typically observed in non-REM sleep, which clearly stand out from the background rhythm, usually differing in frequency and/or amplitude. Compared to phase B*s*, phase A*s* can be composed of slower, higher-voltage rhythms, faster lower-voltage rhythms, or by mixed patterns including both. Although EEG patterns appearing in CAP phase A are not strictly stereotyped, they may include:

- Delta bursts
- Vertex sharp transients
- K-complex sequences with or without spindles
- Polyphasic bursts
- K-alpha
- Intermittent alpha
- EEG arousals

6. CAP Phase A EEG events

6.1. Delta bursts (Fig. 2)

The EEG delta burst is a sequence of at least two waves in the frequency bandwidth ranging from 0.5 to < 4 Hz and with an amplitude 1/3 higher, or more, than the background activity. Delta bursts are most prominent in the fronto–temporal regions. They may appear in consolidated stage 2, and become increasingly common in stages 3 and 4 sleep. Compared to the background EEG delta rhythm of stages 3 and 4, delta bursts tend to be lower in frequency.

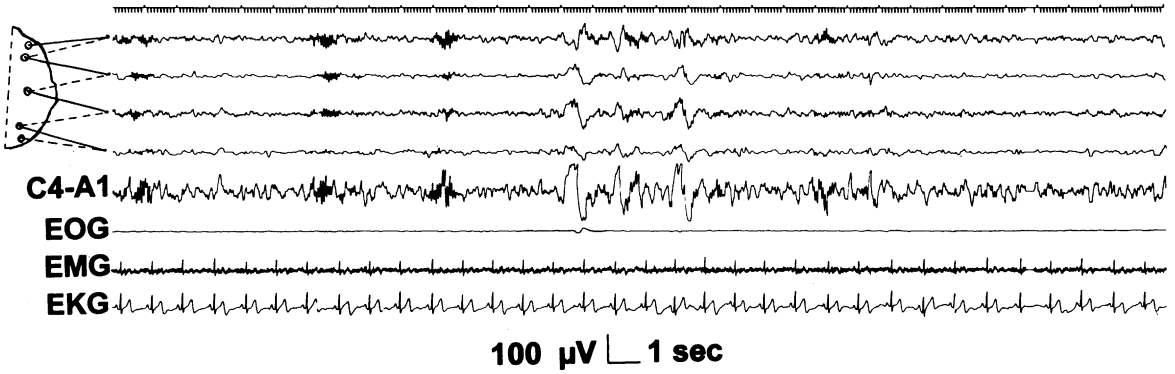

Fig. 4. K-complexes sequences associated with spindles in stage 2 sleep. Top 5 channels: EEG derivation as in Fig. 2.

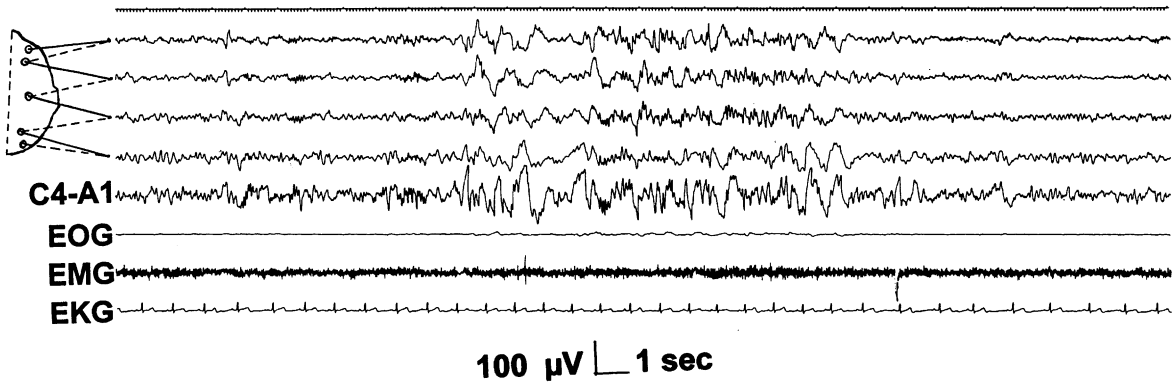

Fig. 5. Polyphasic burst in stage 2 sleep. Top 5 channels: EEG derivation as in Fig. 2.

6.2. Vertex sharp transients (Fig. 3)

Vertex sharp transients are EEG potentials of 50–200 ms duration and variable amplitude (up to 250 μV) expressed maximally on derivations at the central vertex areas. Sequences of vertex sharp transients, composed of two or more repetitive potentials lasting 2 s or more, often appear at the transition from stage 1 to stage 2 sleep.

6.3. K-complex sequences (Fig. 4)

This is a series of two, or more, consecutive K-complexes. Each K-complex presents a bi-/triphasic pattern consisting of an initial rapid negative component followed by a slower positive wave. The K-complex may be mixed with or followed by a sleep spindle. The duration of a single K-complex ranges from 0.5 to 2 s; therefore, a K-complex sequence duration is generally >2 s. K-complex sequences can appear in sleep stages 2, 3, and 4.

6.4. Polyphasic bursts (Fig. 5)

Polyphasic bursts are clusters of high-voltage delta waves, intermixed with theta, alpha or beta rhythms. Polyphasic bursts can include two or more delta peaks and occur in sleep stages 2, 3, and 4. However, polyphasic bursts most commonly appear in stage 2, especially before REM sleep onset.

6.5. K-alpha (Fig. 6)

K-alpha is composed of a K-complex followed immediately by an alpha burst. It has an overall duration of 2 s or more.

6.6. Intermittent alpha (Fig. 7)

The alpha EEG rhythm (8–13 Hz), usually prominent in tracings from posterior derivations is commonly recorded from occipital areas. At sleep onset, the alpha rhythm field tends to spread anteriorly, then in sleep stage 1 it fragments into intermittent sequences, and finally, as sleep progresses, it disappears. Alpha EEG activity may also increase in amplitude and decrease in frequency just before it vanishes. In addition to occurring at sleep onset, intermittent alpha may appear when stage 1 reemerges and during REM sleep.

6.7. EEG Arousals (Fig. 8)

EEG arousals are sudden frequency shifts toward faster rhythms (theta, alpha, beta, but not spindles) that shortly interrupt sleep continuity for ≥ 3 s.

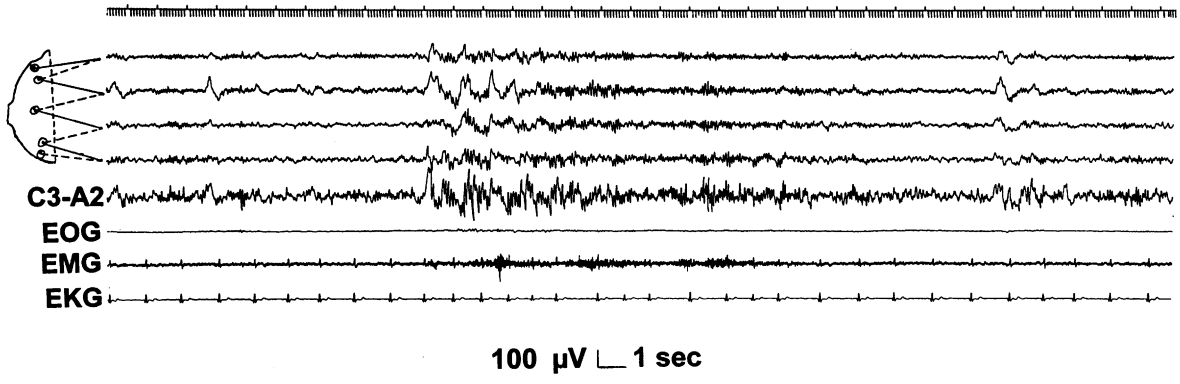

Fig. 6. K-alpha complex in stage 2 sleep. Top 5 channels: EEG derivation as in Fig. 3.

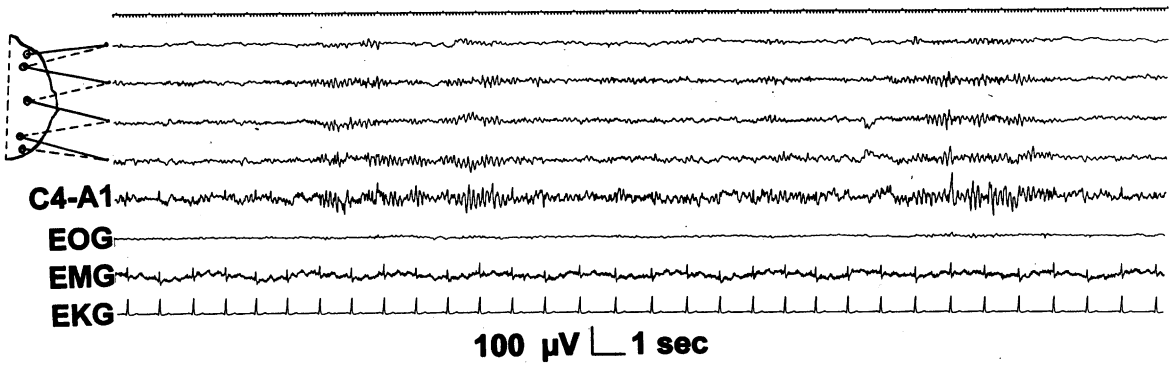

Fig. 7. Intermittent alpha rhythm in stage 1 sleep. Top 5 channels: EEG derivation as in Fig. 2.

7. Requirements for scoring a CAP sequence

The identification of CAP should be preceded by the definition of sleep stages according to the conventional criteria.

7.1. Onset and termination of a CAP sequence

A CAP sequence is composed of a succession of CAP cycles. A CAP cycle is composed of a phase A and the following phase B (Fig. 1). All CAP sequences begin with a phase A and end with a phase B. Each phase of CAP is 2–60 s in duration.

7.2. Non-CAP

The absence of CAP for >60 s is scored as non-CAP (Fig. 9). An isolated phase A, (that is, preceded or followed by another phase A but separated by more than 60 s), is classified as non-CAP (Fig. 10). The phase A that terminates a CAP sequence (Fig. 11) is counted as non-CAP. This transitional phase A bridges the CAP sequence to non-CAP.

7.3. Minimal criteria for the detection of a CAP sequence

CAP sequences have no upper limits on overall duration and on the number of CAP cycles. However, at least two consecutive CAP cycles are required to define a CAP sequence. Consequently, three or more consecutive phase A*s* must be identified with each of the first two phase A*s* followed by a phase B (interval <60 s) and the third phase A followed by a non-CAP interval (>60 s). Fig. 11 illustrates a CAP sequence starting with a phase A but interrupted at the end of the second phase B, while the third phase A is excluded from the CAP sequence because CAP sequences must contain a succession of complete CAP cycles (phase A + phase B).

7.4. General rule

A phase A is scored within a CAP sequence only if it precedes and/or follows another phase A in the 2–60 s temporal range. CAP sequence onset must be preceded by non-CAP (a continuous non-REM sleep EEG pattern for >60 s), with the following three exceptions. There is no temporal limitation: (1) before the first CAP sequence arising in non-REM sleep; (2) after a wake to sleep transition; (3) after a REM to non-REM sleep transition.

7.5. Stage shifts

Within non-REM sleep, a CAP sequence is not interrupted by a sleep stage shift if CAP scoring requirements are satisfied. Consequently, because CAP sequences can extend across adjacent sleep stages, a CAP sequence can contain a variety of different phase A and phase B activities (Fig. 12).

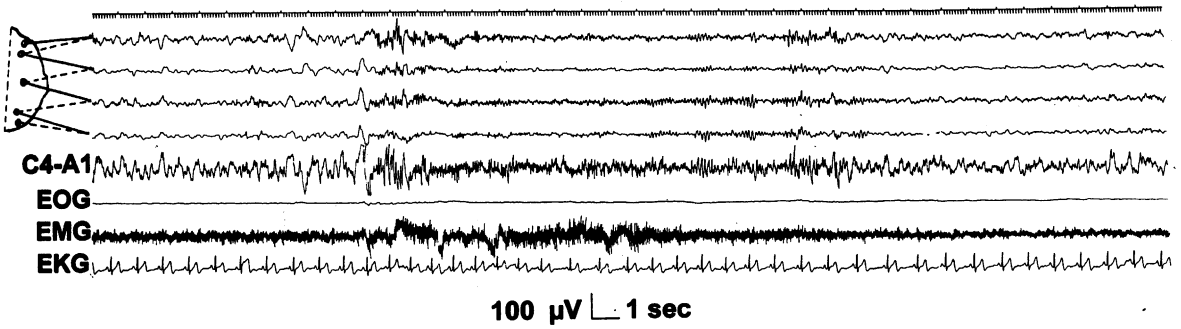

Fig. 8. Arousal preceded and followed by sleep. Top 5 channels: EEG derivation as in Fig. 2.

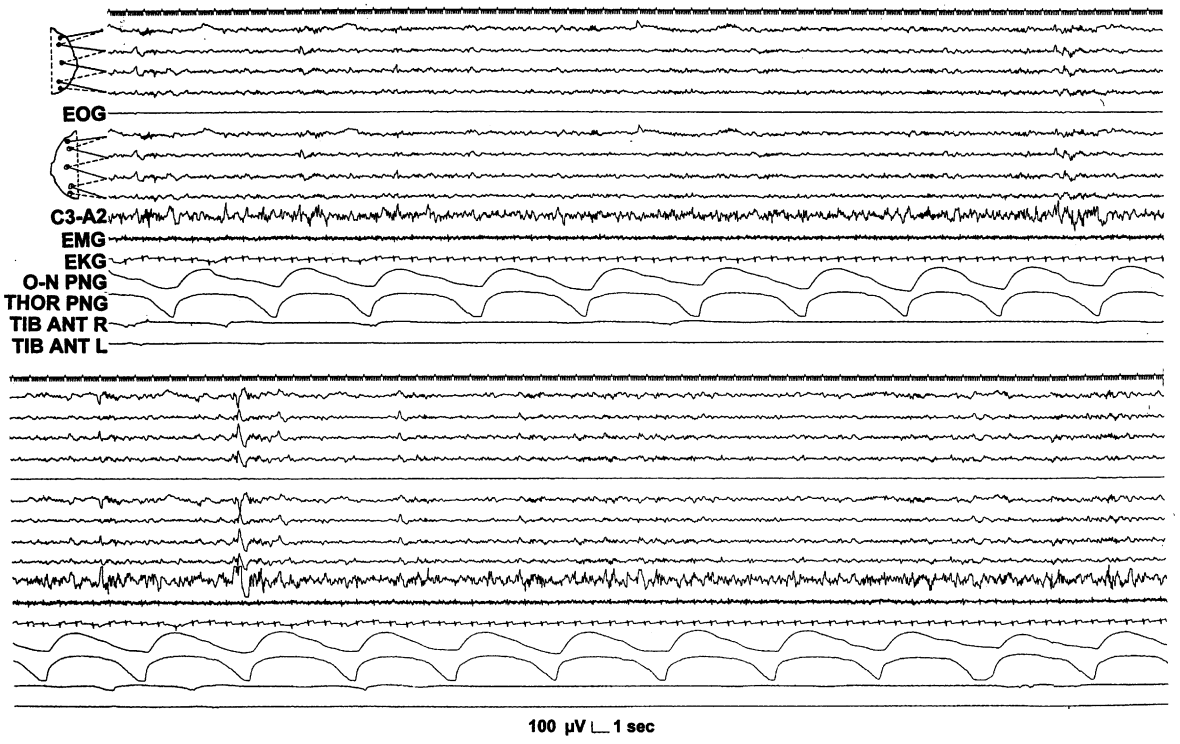

Fig. 9. A long stretch of non-CAP in stage 2 sleep. EEG in channels 1–4 and 6–9 from top to bottom as in Fig. 1, (channels 1–4 and 8–11). O–N PNG: oronasal airflow; THOR PNG: thoracic pneumogram; TIB ANT R: Tibialis anterior right; TIB ANT L: Tibialis anterior left.

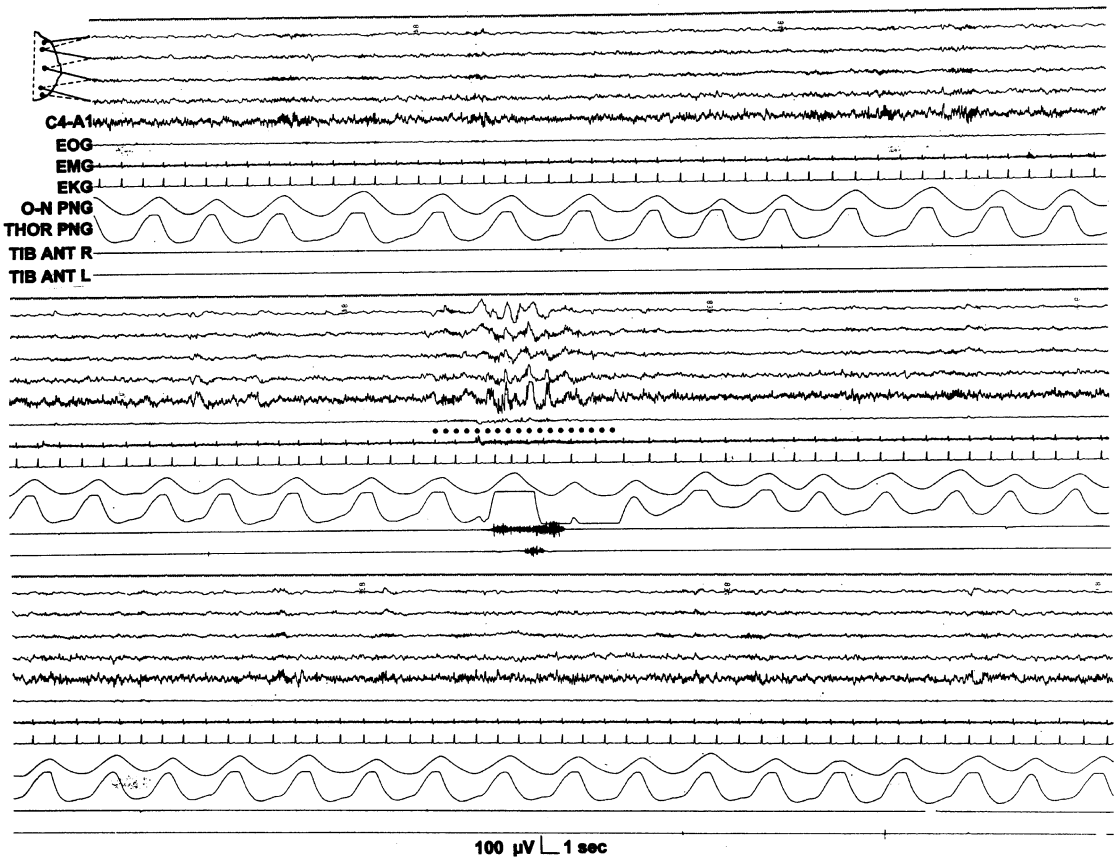

Fig. 10. Isolated phase A preceded and followed by a low-voltage, mixed frequency EEG background for >60 s. EEG derivation as in Fig. 2.

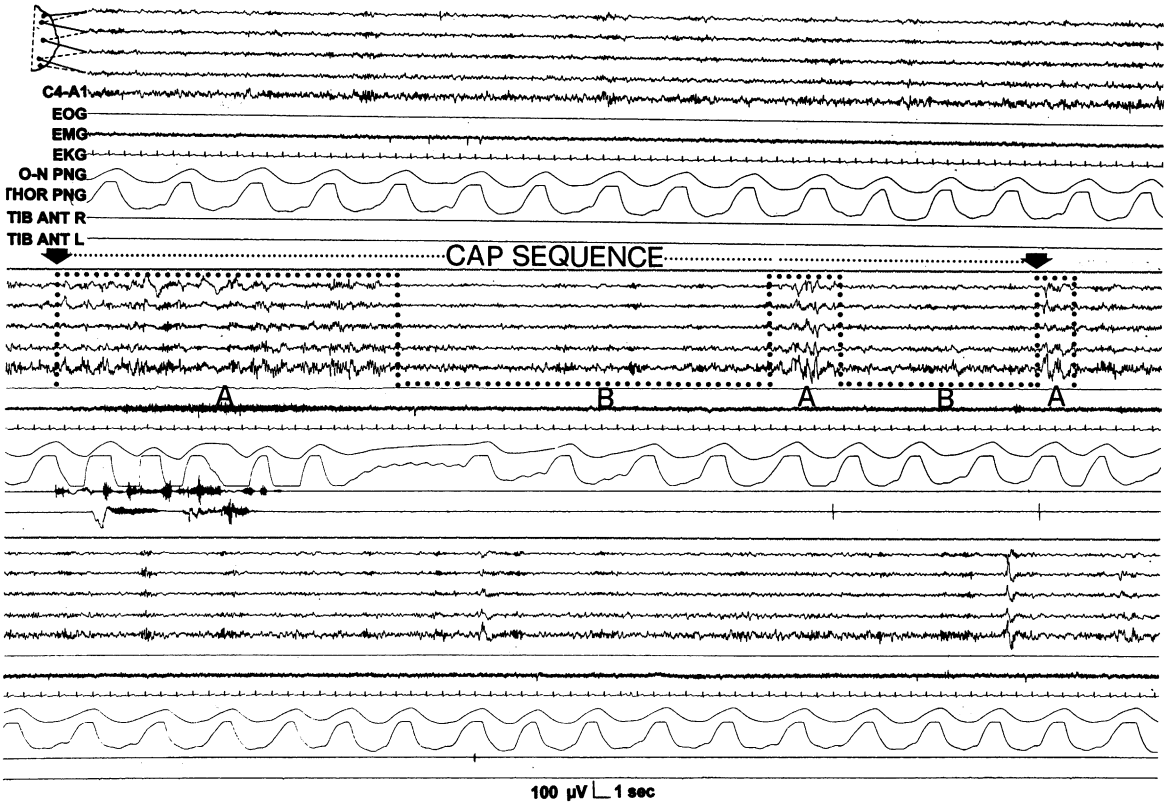

Fig. 11. Consecutive stretches of non-CAP (top), CAP (middle), and non-CAP (bottom). The middle session illustrates the minimal requirements for the definition of a CAP sequence (at least three phase As in succession). The CAP sequence, confined between the two black arrows, is outlined by black-spot boxes. The phase As are identified by bottom open boxes; the phase Bs by top open boxes. The third phase A followed by non-CAP is not included in the CAP sequence. EEG derivation as in Fig. 2.

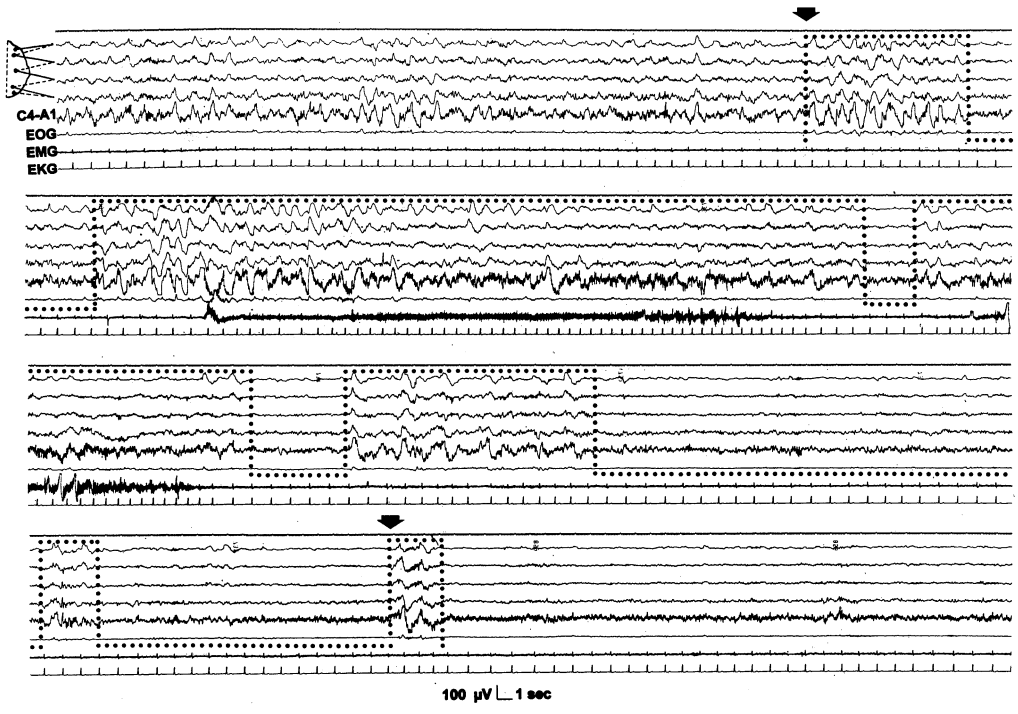

Fig. 12. A CAP sequence (between black arrows) across a stage shift from deep to superficial non-REM sleep. Compared to the other phase As, the second phase A of the sequence is unusually extended (45 s). EEG derivation as in Fig. 2.

7.6. REM sleep

CAP sequences commonly precede the transition from non-REM to REM sleep and end just before REM sleep onset (Fig. 13). REM sleep is characterized by the lack of EEG synchronization; thus phase A features in REM sleep consist mainly of desynchronized patterns (fast low-amplitude rhythms), which are separated by a mean interval of 3–4 min. Consequently, under normal circumstances, CAP does not occur in REM sleep. However, pathophysiologies characterized by repetitive phase A*s* recurring at intervals <60 s (for example, periodic REM-related sleep apnea events), can produce CAP sequences in REM sleep.

7.7. Movement artifacts

Body movements can trigger or interrupt a CAP sequence. Body movements linked to one or more phase A*s* in the temporal range of 2–60 s, can be included within the CAP sequence if other scoring criteria are met (Fig. 14).

8. Recording techniques and montages

CAP is a global EEG phenomenon involving extensive cortical areas. Therefore, phase A*s* should be visible on all EEG leads. Bipolar derivations such as Fp1-F3, F3-C3, C3-P3, P3-O1 or Fp2-F4, F4-C4, C4-P4, P4-O2 guarantee a favorable detection of the phenomenon. A calibration of 50 μV/7 mm with a time constant of 0.1 s and a high frequency filter in the 30 Hz range is recommended for the EEG channels. Monopolar EEG derivations (C3-A2 or C4-A1 and O1-A2 or O2-A1), eye movement channels and submentalis EMG, currently used for the conventional sleep staging and arousal scoring, are also essential for scoring CAP. For clinical studies, airflow and respiratory effort, cardiac rhythm, oxygen saturation, and leg movements should be included as part of standard polysomnographic technique.

9. CAP Phase A boundaries

9.1. Amplitude limits

Changes in EEG amplitude are crucial for scoring CAP. Phasic activities initiating a phase A must be 1/3 higher than the background voltage (calculated during the 2 s before onset and 2 s after offset of a phase A). However, in some cases, a phase A can present ambiguous limits due to inconsistent voltage changes. Onset and termination of a phase A are established on the basis of an amplitude/frequency concordance in the majority of EEG leads. The monopolar derivation is mostly indicated when scoring is carried out on a single derivation (Fig. 14). All EEG events which do not meet clearly the phase A characteristics cannot be scored as part of phase A (Fig. 15).

9.2. Temporal limits

The minimal duration of a phase A or a phase B is 2 s. If two consecutive phase A*s* are separated by an interval <2 s, they are combined as a single phase A. If they are separated

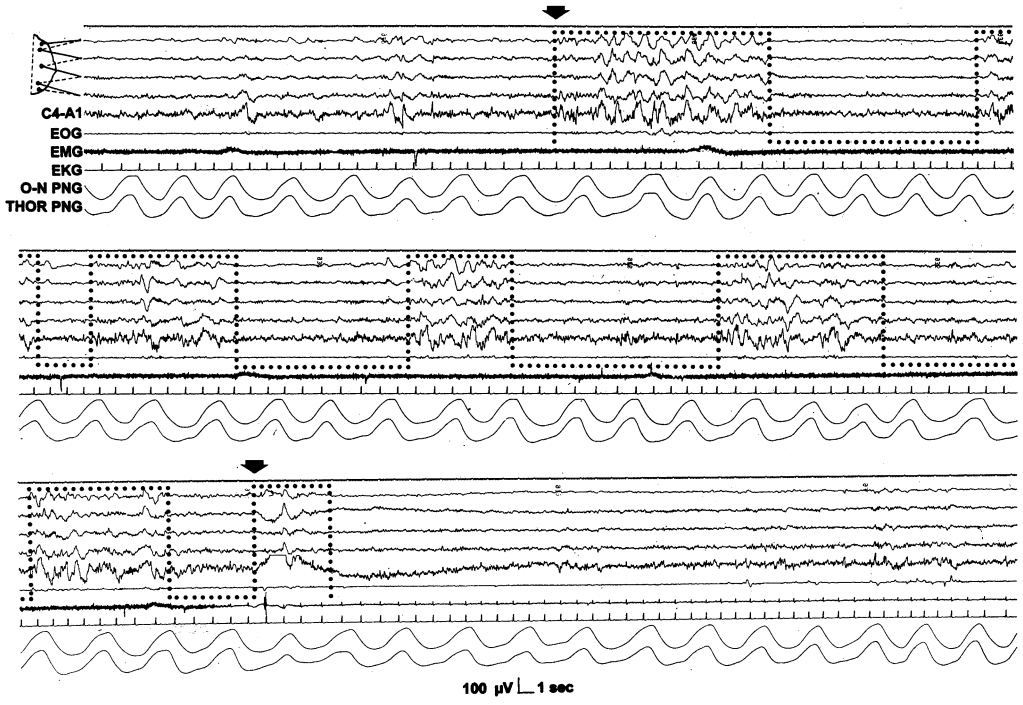

Fig. 13. A CAP sequence (between black arrows) associated with a transition from non-REM to REM sleep. EEG derivation as in Fig. 2.

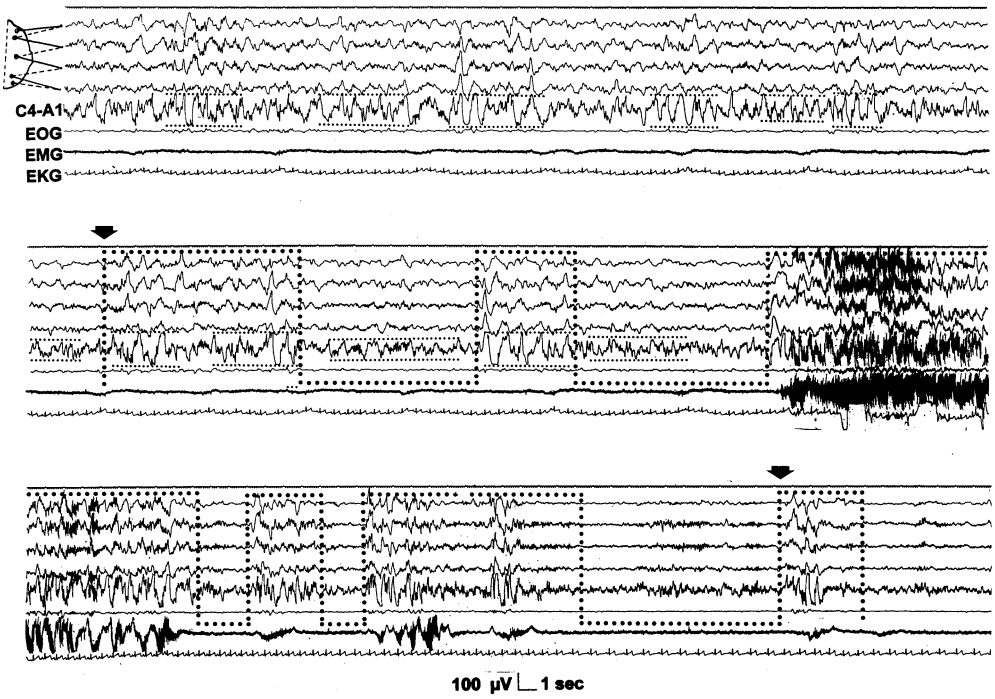

Fig. 14. A CAP sequence confined within the two black arrows and outlined by black-spot boxes (middle and bottom stretches). The top stretch is scored as non-CAP lacking the required amplitude difference (1/3) between the phasic event and the background rhythm (as illustrated by the small black spots reported on the C4-A1 channel). The movement artifact (middle stretch) is included in the CAP sequence. EEG derivation as in Fig. 2.

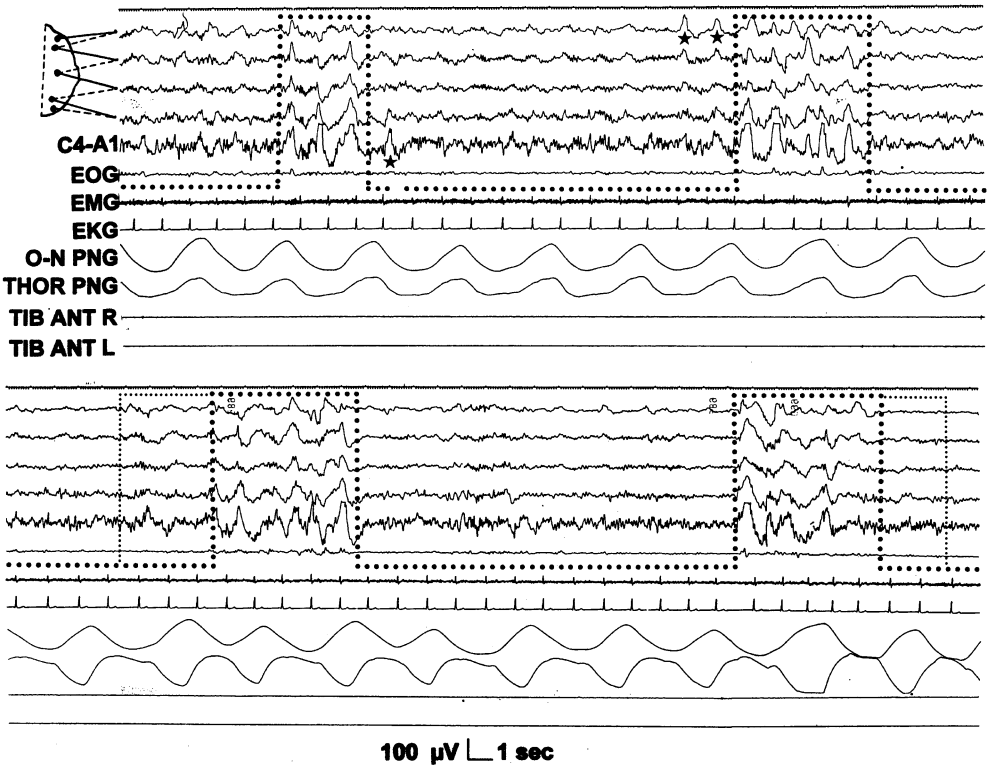

Fig. 15. Four phase A*s* with uncertain boundaries. The omitted portions are indicated by stars (upper session) or by small-spot boxes (lower session). EEG derivation as in Fig. 2.

by a ≥2 s interval, they are scored as independent events (Fig. 16).

10. CAP Phase A morphology

Phase A activities can be classified into three subtypes. Subtype classification is based on the reciprocal proportion of high-voltage slow waves (EEG synchrony) and low-amplitude fast rhythms (EEG desynchrony) throughout the entire phase A duration. The three phase A subtypes are described below (Fig. 17).

- Subtype A1. EEG synchrony is the predominant activity. If present, EEG desynchrony occupies <20% of the entire phase A duration. Subtype A1 specimens include delta bursts, K-complex sequences, vertex sharp transients, polyphasic bursts with <20% of EEG desynchrony.
- Subtype A2. The EEG activity is a mixture of slow and fast rhythms with 20–50% of phase A occupied by EEG desynchrony. Subtype A2 specimens include polyphasic bursts with more than 20% but less than 50% of EEG desynchrony.
- Subtype A3. The EEG activity is predominantly rapid low-voltage rhythms with >50% of phase A occupied by EEG desynchrony. Subtype A3 specimens include K-alpha, EEG arousals, and polyphasic bursts with >50% of EEG desynchrony. A movement artifact within a CAP sequence is also classified as subtype A3.

So far, alpha activity has been considered as the highest expression of EEG synchrony in sleep stage 1. In the light of this, intermittent EEG alpha is classified as subtype A1. However, because EEG alpha is a constituent activity of stage 1 and REM sleep and can occur in stages 2, 3 and 4, intermittent EEG alpha may be scored separately as a specific phase A pattern.

Slow rhythms represent the main features of subtypes A1. Within subtypes A2 and A3, slow rhythms mostly prevail in the initial part of phase A. Other patterns can, however, occur; for example, an initial onset of fast rhythms or a mixture of both EEG synchrony and EEG desynchrony (Fig. 18).

Different phase A subtypes can occur within the same CAP sequence (Fig. 19). Subtype A1 is most common as sleep EEG synchrony increases (from light to deep non-REM sleep) and when synchrony predominates (stages 3 and 4). Subtypes A2 and A3 are mostly concentrated as sleep-related brain activity progresses from synchrony to greater desynchrony (for example, in stage 2 preceding the onset of REM sleep).

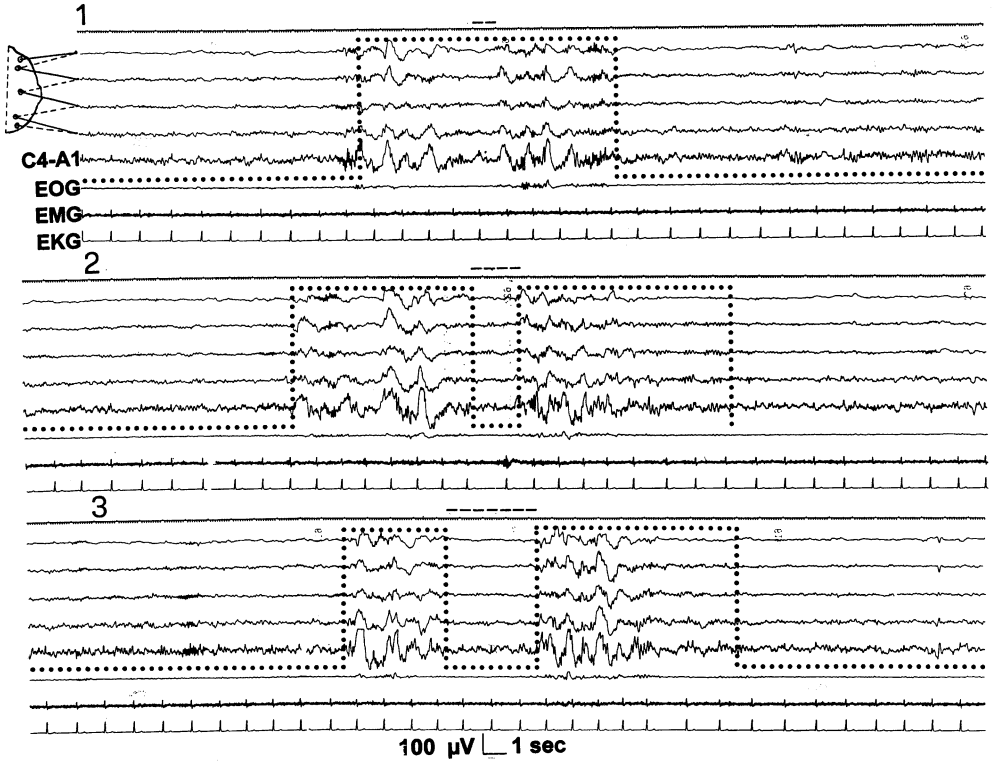

Fig. 16. Three stretches of double phase As. The top couple is scored as a single phase A being the interval <2 s. The middle and bottom couples are scored as independent phase As. EEG derivation as in Fig. 2.

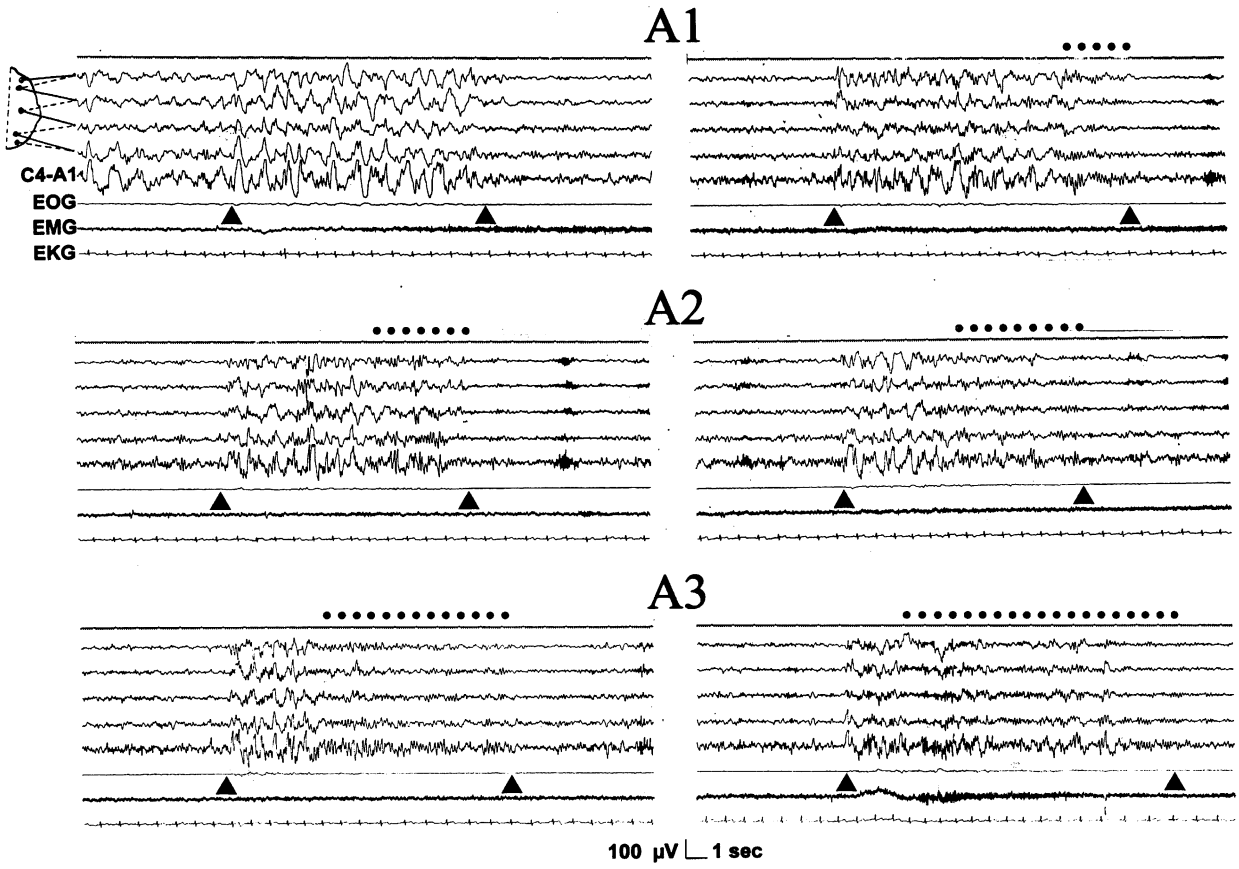

Fig. 17. Phase A subtypes. The dotted spots indicate the fast low-amplitude portion of the phase A. EEG derivation as in Fig. 2.

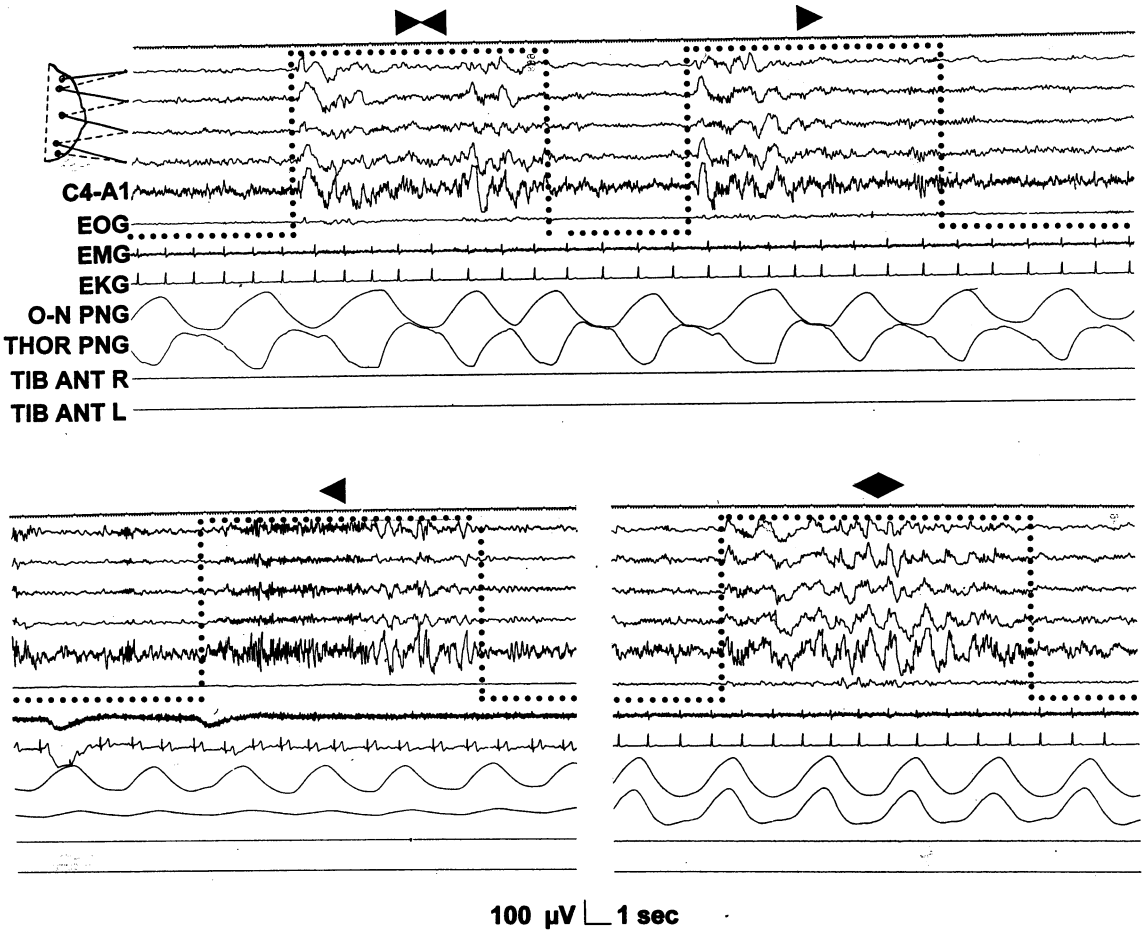

Fig. 18. Four different phase A configurations. The black marks above each phase A outline the overall rhythm assemblage. EEG derivation as in Fig. 2.

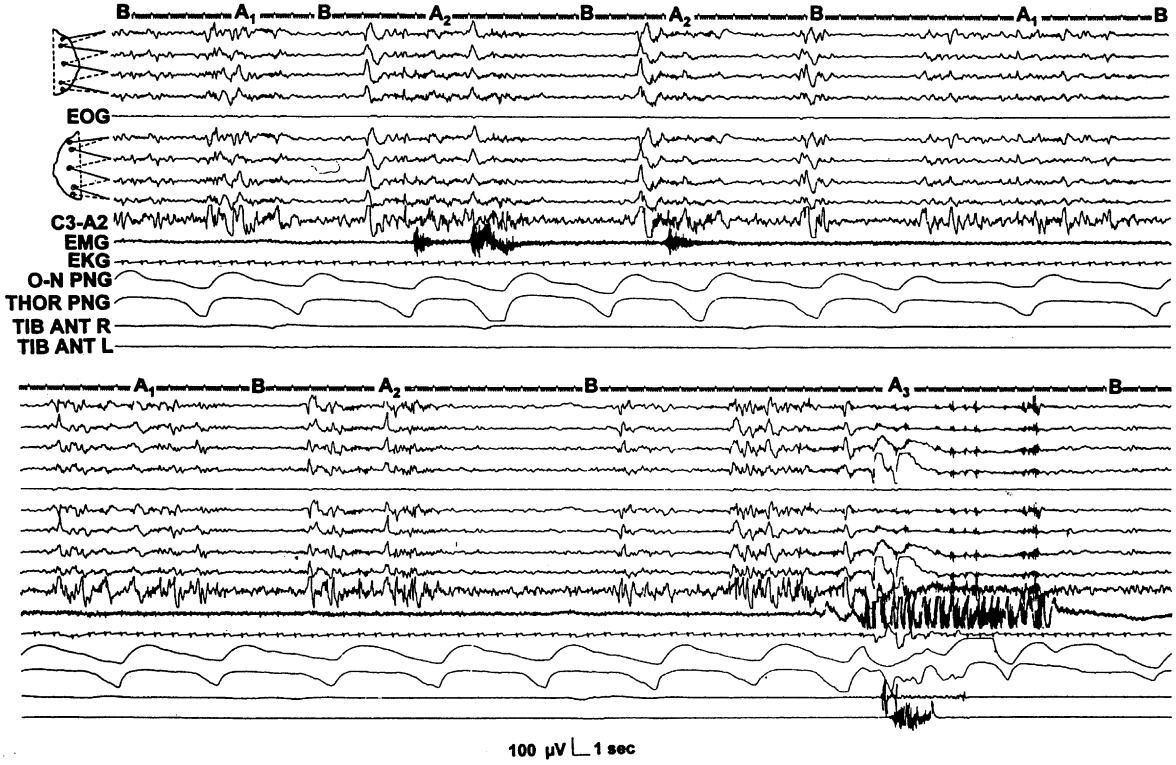

Fig. 19. A CAP sequence including all subtypes of phase As. EEG derivation as in Fig. 9.