Normal Neonatal EEG

11

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In this chapter, the peculiar aspects of neonatal EEG are discussed, alongside with the recording modalities and the characteristic and age-specific electroencephalographic physiological patterns of the newborn, from preterm birth to the end of the neonatal period. In the Appendix, the terms utilized to describe the neonatal EEG will be defined.

The iconographic material is taken from electroencephalographic exams performed during daily clinic practice at V. Buzzi Children Hospital, in Milan (Pediatric Neurology Unit and Neonatal Intensive Care Unit). The children to whom the iconography refers have been evaluated by at least one of the authors and are not affected by any neurological condition.

11.1 Neonatal EEG Features

The EEG is a relatively easy, reproducible, non-traumatic method of functional exploration of the cortical and subcortical cerebral activity. It can be performed also at the patient's bed and with ventilatory assistance. Together with clinical signs and neuroimaging investigation, the EEG allows a global and dynamic evaluation of the brain functioning, and it has also an early prognostic value since the neonatal period [1]. It is important to underline the French author's statement in which a methodological fundamental message is contained: especially in the neonatal period, compared to all the other periods of life, the EEG interpretation cannot be made regardless of the clinical and neuroradiologic data. The integration of EEG characteristics, anamnestic data with gestational age (GA) and conceptional age (CA), clinical features (neurological examination and behavioral state during the EEG recording), and morphological elements (cerebral ultrasound and magnetic resonance image (MRI) is an essential condition for an accurate definition of the functional state of the brain of the newborn. In addition, the fetal and neonatal brain maturation from the 24th week of GA up to the term age is responsible for significant modifications of neonatal behavioral and EEG patterns. Therefore, the reference parameters vary, from prematurity to the at term age, depending on the CA.

11.2 Historical References

The first EEG recordings were performed by Hans Berger in 1929, becoming more and more frequent and technically satisfactory during the following decades. Only at the end of the 1950s, thanks to the contribution of French authors in particular, the electric patterns of preterm and full-term newborns were relatively defined. The peculiarities of cerebral electrical activity were emphasized, such as the presence of "inactive" periods, i.e. without electrical activity, of longer duration, the greater the prematurity; moreover the different patterns and graphic elements were also defined depending on the different CA. In parallel, since the second half of the 1950s and in the following decade, German authors focused their interest on the behavioral patterns of the newborn: wake, sleep, and different types of sleep states, defining their characteristics and relative percentages, in the development of the brain from prematurity to the end of gestation.

From the second half of the 1960s, but especially from the second half of the 1970s, thanks to the contribution of Parmelee et al. [2], Dreyfus-Brisac and Monod [3], Monod and Tharp [4], Watanabe et al. [5, 6], Tharp et al. [7], and Lombroso [8], a relatively standardized and adopted "normative" is in fact available, regarding the technical characteristics of recording and the normal and pathological EEG patterns in the premature and term infant, to which we sub-

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stantially refer today. Within the aforementioned papers, the interested reader can find the historical bibliographic references relating to the EEG in the neonatal period.

11.3 Qualitative Analysis of the Signal

The qualitative analysis and interpretation is based on the visual examination of the EEG [9, 10]. It involves the observation and definition of the EEG background activity and of the typical developmental EEG features specific to each CA. Therefore, the knowledge (of the examiner) and the possibility to define the parameters of "normality" must take into account the individual variability and influence that extra-neurological factors may have on the EEG patterns. This becomes the conditio sine qua nonotherwise it is impossible to correctly address and define what is pathological.

Related to the anatomic-functional brain maturation, it is known that from the 24th week of GA up to the period corresponding to the term age, there are changes in both the clinical behavior and the electro-cerebral activity, which vary specifically for epochs of 2 weeks. Literature is consistent in defining the normal findings of a recording at different conceptional ages, the severity grade of the brain impairment, the prognostic value of serial recordings at standardized times, the diagnostic meaning of some specific EEG patterns, the definition of the EEG findings of the epileptic seizures (which may be both electroclinical and electrographic only seizures), the ability to evaluate the effects of anticonvulsant therapy taking into account the phenomenon of the "electroclinical dissociation," and the possibility of obtaining information on the cerebral functioning of patients which are difficult to examine (newborns in coma or curarized). Moreover, extreme caution is necessary in formulating a judgment of abnormal recording, particularly in the context of extreme prematurity where there could be a modest disproportion between the observed electrical pattern and the CA of reference.

Since we discuss the normal criteria of the neonatal EEG in this chapter, it is necessary to point out the concept of "normality" at different gestational ages. Given that a physiological pregnancy has a duration of 38–42 weeks, it seems paradoxical to speak of "normality" in case of a baby born at 24 or 25 weeks of GA. On the other hand, the scientific progress in the perinatal medicine has led to a significant increase in the number of extremely preterm newborns; therefore, it is essential to investigate features of normal brain functioning even in the preterm newborns less than 27 weeks of GA.

These are obviously "extreme" clinical conditions often associated with a "low or very low birth weight." However, extreme prematurity could also be due to a maternal cause, and it is not uncommon to observe apparently healthy extremely premature infants (not affected by major neurological pathologies). In these cases, the knowledge and definition of "normality" features, while taking into account the individual variability and the extra-neurological conditions, is the essential prerequisite for tackling the problem of "pathology."

In summary, a methodological approach to interpreting the neonatal EEG that can be agreed upon is the one proposed by Janet E. Stockard-Pope [11], to which we add, however, the two points related to the clinical condition of the patient. The EEG is in fact a technique whose diagnostic potential is strongly enriched when it is strongly integrated into the general (clinical-neurologic-neuroradiological) context of the newborn:

- To know the GA and CA.
- To define the clinical condition.
- To define the cerebral ultrasound picture.
- To define the behavioral state.
- To define the polygraphic EEG findings according to the conceptional age and the behavioral state, with particular reference to the spatial and temporal organization of the background EEG activity, to the synchrony, to the presence of specific age patterns, to the reactivity, and to the EEG-behavioral state.

With some simplification, the gestalt approach to the neonatal EEG, from the extreme prematurity to the term age, involves the definition of the findings during the inactive EEG epochs and of the findings during the epochs with electrical activity and their evolution and modification over the weeks.

Only after the acquisition of such a methodological approach, it will be possible to take into consideration the characteristics of the pathological EEGs [12–14].

Before concluding this first introductory part, it is necessary to point out the research carried out by the group of Mizrahi, Kellaway, and Hrachovy of the University of Houston, Texas [15], from the end of the 1990s on the attempt to develop automatic and semiautomatic signal analysis systems in this particular field of application: prolonged monitoring in infants at risk of seizures. This approach is outside the scope of this manual, but the reader might find further information in Karayannis et al. [16]. Finally, Stevenson and Boylan [17] have reviewed and deepened the topic of automated seizure detection concluding that despite recent progress, it is not yet possible to apply these technologies into routine clinical practice.

11.4 Registration Techniques

The EEG recording in the neonatal period represents some peculiar difficulties related to the type of patient and the environment in which it is registered (incubator, thermal cradle).

The reader can refer to the guidelines of the American Clinical Neurophysiology Society (ACNS) [18, 19], to the

ones of the International Federation of Clinical Neurophysiology [20], and to the work of Chang and Tsuchida on continuous EEG monitoring [21].

Here, we only want to highlight some significant aspects.

11.5 Preparation of the Newborn

The behavioral state of the newborn is a very important variable to consider in order to perform a recording that includes an entire cycle of spontaneous sleep and quiet wake phases, if age and general clinical conditions allow it. Therefore, it is suggested to breastfeed the newborn before the recording, provide a diaper change, and start recording even when awake but prolong it until the required behavioral states are achieved.

11.6 Positioning of the Electrodes

Chlorinated silver cup electrodes are used, with electroconductive paste, applied with ring-shaped patches, better if then fixed with a net that covers the scalp collecting the wires toward the electroencephalograph head. A cotton ball is placed above each electrode, under the patch, to improve grip. In the newborn, especially in a thermal cradle, the use of collodion (toxic) is prohibited.

A rapid application variant, used in our laboratory, consists of "preborn" button electrodes, inserted into perforated rubber bands. Needle electrodes are not recommended; being traumatic, they can be a source of infection.

The electrodes are positioned according to the International System 10–20 [22], modified for the newborn, taking into account both the size of the skull, especially in the extreme premature babies, and the immaturity of the frontal lobes of the newborn that do not extend so anterior to the skull.

Although it is obvious that the higher the number of electrodes on the scalp, the finer the signal can be, in our experience, nine head positions can be considered sufficient to acquire a properly differentiated signal in relation to the spatial organization.

No more than 8–10 electrodes are used: generally F3-4, C3-4, O1-2, T3-4, Cz., connected according to a double longitudinal montage (F4-C4, C4-O2, F4-T4, T4-O2, F3-C3, C3-O1, F3-T3, T3-O1) and a transverse montage that includes the vertex (T4-C4, C4-Cz, Cz-C3, C3-T3). Furthermore, an additional extracephalic reference lead is applied.

Before applying the electrodes, the baby's scalp is prepared with a slight abrasion in each electrode seat with a medium abrasive gel using the cotton end of an applicator stick; this can cause a slight erythema but it is only temporary and transitory.

For prolonged EEGs, it is necessary to apply a new dose of conductive paste to the cup electrodes—once or twice a day.

The optimal recording time of an examination is not less than 90 minutes, and therefore usually it takes at least 2 hours, considering the preparation time of the newborn and the adjustment of the child to the optimal recording. Even for the premature baby, the recording should not take less than 40 min and must allow to obtain relatively stable periods with a continuous and discontinuous electric EEG pattern.

Generally the reactivity of the child, and of the EEG traces, must be systematically studied at the end of the recording with auditory stimuli (hand clapping) or tactile stimuli; the technician must be constantly present during the recording to make the necessary adjustments in the surrounding environment (artifacts) and for the newborn care.

The EEG parameters used in our laboratory are high-pass filter of 0.53 Hz; low-pass filter of 30 Hz; notch filter for network noise, active; signal sensitivity of 100 mcV for 10 mm; and scrolling speed of 15–30 mm/s.

11.7 Polygraphic Parameters

In clinical practice, with the exception of specific medical indications, the polygraphic parameters are not recorded in critically ill neonates and in extreme preterm neonates (especially if intubated) that must be handled with extreme caution. In the others, the acquisition of polygraphic parameters is necessary to document and characterize the different behavioral states. Until the third month of post-conceptional age (PCA), cup electrodes are used with electroconductive paste, fixed with a plaster.

- Electrooculogram (EOG). The electrodes are positioned laterally to the external chant, on the two sides, respectively, above and below the median, to acquire both the lateral and the vertical eye movements.
- Recording parameters used are high-pass filter of 0.53–1.6 Hz, low-pass filter of 30 Hz, and signal sensitivity, to be adapted according to the deflection caused by the movement of the ocular globe—generally 100–200 mcV for 10 mm.
- Electromyogram (EMG). Muscle activity can be documented by placing a pair of skin electrodes under the chin on the chin muscle.
- The recording parameters used are high-pass filter of 5.0 Hz, low-pass filter of 70 Hz, and sensitivity, to be adapted according to the deflection caused by the suction movement—generally 100–150 mcV for 10 mm.
- Electrocardiogram (ECG). An electrode is located above the midline of the thorax and refers to other one in the left side of the thorax for recording a single channel that allows to identify the heart rhythm and especially a waveform certainly due to the electrical deflection of cardiac origin (see artifacts and constantly low-voltage EEG trace).
- The recording parameters used are high-pass filter of 5.0 Hz, 15 Hz of low-pass filter, and sensitivity, to be

modified according to the amplitude and the acquired waveform that varies with respect to the positioning of the electrodes (since the ECG is a wide signal, a sensitivity of 700–800 mcV is used).
- Respiratory activity. The respiratory rate is recorded at the thoracic and abdominal level using band transducers able to appreciate chest wall movements; in addition, the measurement of the airflow from the nostrils and the mouth is associated allying thermocouple devices placed under the nostrils and the registration of the saturation of O_2 and CO_2 by means of a distal oximeter.
- The recording parameters used are high-pass filter of 0.016 Hz, low-pass filter of 15 Hz, and sensitivity, to be adapted according to signal characteristics (150–200 mcV).
- Other nonstandard parameters can be recorded in particular clinical conditions: measurement of systemic blood pressure, global body movements, and contact EMG on different muscle groups.

11.8 Digital Video EEG

In recent years, with particular reference to the study of the semiology of neonatal seizures, considerable interest has been placed on this type of method that allows to obtain a video recording synchronized to the EEG recording. In order to obtain a good recording, it is essential to have a proper preparation of the surrounding environment: in particular, it is important to check temperature and lighting and avoid interference between the recording instruments and those used for the newborn care. During paroxysmal events and in any case where unusual events occur, nursing staff should not interfere with video recording, and the newborn should be kept uncovered to allow observation of the face and limbs.

The EEG technician, adequately trained in the management of the newborn, has the task of recording important events for the interpretation of the EEG. It is up to him, in any case, to prepare and properly follow the EEG registration. The video-EEG does not replace the human eye but provides the possibility of an off-line review of what happened during the recording phase [14, 23].

11.9 Maturation of Behavioral and EEG Patterns: From Prematurity to the End of the Neonatal Period

11.9.1 Behavioral Patterns

In the term infant, it is possible to recognize "behavioral states" with cyclic and predictable trends, defined on the basis of the presence of specific motor, neurovegetative, and affective-relational behaviors.

These states defined by Prechtl and Beintema [24], on the basis of changes in breathing, eye movements, body movements, and crying, are clearly identifiable from the 37th week of GA. Each specific behavioral state corresponds to a specific cerebral electrical activity.

State I: Regular breathing, eyes closed, and no movement of the body (quiet sleep)
State II: Irregular breathing, closed eyes, and small movements of the body (active sleep)
State III: Open eyes and rare and slow movements of the body (quiet alert)
State IV: Open eyes and movements of great amplitude (active alert)
State V: Open or closed eyes, intense motor activity, and crying

In the preterm newborns, the behavioral states are less clearly defined. In infants aged under 28 weeks of GA, sleep and wakefulness are not always discernible (indeterminate state). Historically, it has originated the statement that a newborn of GA under 27 weeks is never awake and never sleeps [4]. Actually, a clear difference between wakefulness and sleep is only possible from 32 weeks of GA. Before this age, it seems more appropriate to define rest phases and phases of activity (rest-activity cycles). On the other hand, some authors hypothesize the emergence of a rudimentary sleep differentiation even in earlier ages; however, the definition of states is constantly based on the use of the EEG. Vecchierini et al. [25] analyzed the characteristics of EEG and ocular motility in a preterm sample at a conception age of between 24 and 26 weeks and documented the presence of two sleep patterns: the first one characterized by the presence of eye movements and a more continuous cerebral electrical activity of greater amplitude and the second one from the absence of ocular movements and from a more discontinuous and lower-amplitude electrical activity. At 28–31 weeks of GA, from the EEG and polygraphic point of view, we begin to recognize epochs of activity in part similar to the active sleep and alert states recognized in the full newborn, alternating with epochs of "quiet sleep." From 31 to 34 weeks' GA, these epochs of active sleep-wakefulness are more easily identifiable with behavioral and polygraphic parameters and prevail over the phases in which the newborn appears inert and the polygraphic-behavioral parameters suggest a phase of quiet sleep. Only from 35 weeks of GA, a clear differentiation between wakefulness, active sleep, and quiet sleep is recognizable. From 38 to 42 weeks of GA, the behavioral states are stable and well differentiated with progressive reduction of the active sleep phases and parallel increase in the phases of quiet sleep.

Active sleep (REM sleep) corresponds to Prechtl's state II, and it is ontogenetically the most ancient sleep because it

originates from subcortical structures (it originates in the rostral part of the brainstem with projections to the hypothalamus). The newborn shows small-body movements, sometimes smiles or makes facial grimaces, and presents rapid lateral movements of the eyeballs; breathing is irregular and the muscle tone is decreased (especially bulbar muscles). Up to 34 weeks' GA, this is the predominant type of sleep. The full-term newborn falls asleep directly into REM sleep. Two EEG patterns are distinguished within the active sleep cycle. The first is recognizable at the beginning of the cycle: high-voltage continuous (HVC) or mixed activity. The second is called low-voltage irregular (LVI), and it is observed after a non-REM sleep cycle. In some cases, the active sleep that follows a calm sleep appears completely indistinguishable from the wake EEG pattern (activité moyenne).

Quiet sleep (non-REM/NREM sleep) corresponds to a more developed status (Prechtl's state I). It is a more evolved status than the previous one because it originates from the caudal structures of the brainstem with projections to the hypothalamus, to the thalamus, and subsequently into the cortex. It appears well differentiated from the 35th week of GA and is recognizable by the presence of regular breathing (short respiratory irregularities are still possible, especially in infants with respiratory disorders), absence (or rare) of eye movements, and constant tonic muscle activity. Body movements are rare and similar to sursauts. In this behavioural state, two patterns are discernible: the first is called alternating pattern (tracé alternant), and the second is continuous slow-wave pattern [continuous slow waves (CSW) or high-voltage slow (HVS)]. For practical purposes, even at lower GA, the discontinuous patterns are more often associated with states in which the newborn lies motionless with closed eyes, and most of the authors believe that this electroclinical condition can be assimilated to a quiet sleep phase.

Indeterminate (or transitional) is defined as a sleep period that does not meet the criteria described above for active sleep or quiet sleep. It is generally observed just before REM sleep and between REM sleep and quiet sleep.

11.9.2 Physiological EEG Patterns

In general, the EEG recording of the premature infant is characterized by the discontinuity of the brain electrical activity. The recording of the full-term infant, and in any case with a CA over 35–36 weeks, is characterized by the continuity of the electrical activity in all the states [15, 25, 26].

The visual analysis of the neonatal EEG, from prematurity to the term CA, involves in the first instance the definition of the features during either the inactive trace or the traces with electrical activity, with their respective spatial and temporal characteristics. In the context of the so-called developmental process, there is a gradual change from a discontinuous pattern to a continuous one, which simultaneously loses the typical electrical features of the previous CA to be enriched with graphic elements typical of later CA. At the same time, the EEG patterns associated with the different behavioral states of wakefulness and sleep, which are organized proportionally to the CA, must be identified. The comparison of certain shapes and electrical EEG patterns characteristic of the appropriate CA is an indication of behavioral electrical concordance and ultimately of probable physiological functionality of the CNS. On the contrary, the absence of concordance and the alteration of EEG patterns must be at least a suspicion sign of pathology. However, it should be kept in mind that for each CA, typical figures and EEG patterns can coexist with figures and patterns of earlier ages and that the EEG patterns are very sensitive to extracerebral variables. It follows that the conclusion on the EEG recording, especially in preterm babies, should be expressed with caution and based on repeated recordings at appropriate times. Dealing with a full-term infant, in the ideal recording conditions, a complete sleep wake cycle can be obtained during a 60–90 min-EEG recording; wakefulness → active sleep → quiet sleep → wakefulness (sometimes after a quiet sleep cycle it is also possible to observe a second phase of the active sleep with an activité moyenne-like pattern).

A summary of the peculiar EEG features and patterns in the different CA is reported below (see also Table 11.1):

Before 27 weeks GA: EEG recording is characterized by discontinuous electrical activity as follows: short bursts of a duration varying from 1 to 46 s (or more) and with amplitude around 50 μV are interspersed with inactive epochs lasting generally less than 60 s. The presence of slow waves at 0.5–1 Hz of variable amplitude up to over 300 μV, with variable localization, sometimes widespread, often temporal or occipital, mono-/biphasic, often in short sequences, rarely associated with rapid activity at 5–9 Hz that is superimposed on the slow waves when located in the central regions. The presence of isolated high-amplitude and variable morphology frontal sharp waves (200–300 μV). Short burst, diffuse, or temporal and occipital localization of sharp theta activity of high amplitude up to 300 μV might also be observed.

The greater the prematurity, the longer the duration of the epochs in which no electrical activity is recognized on the EEG recording; reciprocally, the greater the prematurity, the lower the duration of the epochs with continuous electrical activity.

Significant interhemispheric synchrony of the bursts. Monomorphic occipital delta, in short runs of a few seconds, bilaterally synchronous and symmetric. Poor or no reactivity of the background EEG activity to stimulations (Figs. 11.1, 11.2, 11.3, and 11.4).

By 27 to 29 weeks GA: EEG recording with an overall discontinuous electric activity, more continuous in active

Table 11.1 Developmental EEG patterns and behavioral states

Conceptional age (week)	Specific waveforms[a]	Continuity of electrical activity and specific patterns[a]	Behavioral state
24–27	Hypersynchronous bursts Occipital delta of 0.5–1 Hz Infrequent central (occipital) delta brushes	Discontinuous tracing No reactivity to stimulation	Undetermined state
28–31	Occipital delta Central delta brushes Rhythmic temporal theta activity Sharp temporal theta bursts	Discontinuous tracing Electrical activity becomes continuous during active sleep No reactivity to stimulation	Active sleep (Wake±/Quiet sleep±)
32–34	Frequent occipital-temporal delta brushes Synchronous occipital delta Rhythmic temporal and alpha bursts Both positive and negative, temporal and Rolandic sharp waves	Discontinuous tracing (in quiet sleep) Continuous tracing in active sleep Inconstant reactivity to stimulation	Active sleep (Wake±) (Quiet sleep±)
35–37	Encoches frontales ASD[b] (infrequent) Infrequent occipital delta brushes Multifocal slow sharp waves	Activité moyenne LVI[c] Tracé alternant Reactive to stimulation	Wake Active sleep Quiet sleep Undetermined/ transitional sleep
38–44	Encoches frontales ASD[b] Isolate Rolandic and temporal sharp waves	Activité moyenne Mixed activity LVI[c] Tracé alternant HVS[d] Reactive to stimulation	Wake Active sleep Quiet sleep Transitional sleep

Adapted from Lombroso [12], Tharp [27], Anders et al. [28], Kellaway [29], Ferrari et al., [30] Mastrangelo et al., [31], André et al. [32]
[a]Both for the specific waveforms and patterns, refer to the following iconography (Figs. 11.1, 11.2, 11.3, 11.4, 11.5, 11.6, 11.7, 11.8, 11.9, 11.10, 11.11, 11.12, 11.13, 11.14, 11.15, 11.16, 11.17, 11.18, 11.19, 11.20, 11.21, 11.22, 11.23, 11.24, 11.25, 11.26, 11.27, 11.28, 11.29, 11.30, 11.31, 11.32, 11.33, and 11.34)
[b]*ASD* anterior slow dysrhythmia
[c]*LVI* low-voltage irregular
[d]*HVS* high-voltage slow

sleep state. Rolandic and occipital delta brushes, in active sleep state. Initial representation of theta rhythmic temporal activity (temporal sawtooth) in sequences (runs) up to 2 s—bilateral symmetric and synchronous occipital delta waves in sequences of variable duration (less than 60″). Less interhemispheric synchrony of the bursts compared to the aforementioned age. Poor or no reactivity of the background EEG activity to stimulations (Figs. 11.5, 11.6, 11.7, 11.8, 11.9, 11.10, 11.11, and 11.12).

By 30 to 34 weeks GA: EEG recording with an overall discontinuous electrical activity during calm sleep, greater representation of continuous epochs during active sleep state.

Frequent occipital and temporal delta brushes in active sleep state (from 33 weeks of CA in quiet sleep)—reduction of temporal theta temporal activity (from 32 weeks of CA) replaced by temporal rhythmic alpha activity that disappears before 35 weeks of CA.

Significant interhemispheric asynchrony (especially in quiet sleep state). Initial reactivity of the background EEG activity to stimulation (Figs. 11.13 and 11.14).

By 35 to 37 weeks GA: continuous electric activity in all the states (mixed activity) in wakefulness/active sleep state, although transient and short periods of low-voltage background EEG activity may occur in quiet sleep state. Reduction of delta brushes with occipital and temporal localization, more evident in quiet sleep state. Frontal sharp waves in sleep state (more often bilaterally synchronous). Initial appearance of anterior slow dysrhythmia (ASD). Isolated multifocal sharp waves. Resumption of the interhemispheric synchrony. Background activity reactive to stimulation (Figs. 11.15, 11.16, 11.17, 11.18, 11.19, 11.20, and 11.21).

More than 38 weeks GA: continuous electrical activity in all states. Frontal sharp waves and ASD more frequent in the transition from active sleep state to quiet sleep state. Isolated Rolandic or temporal spikes. Significant interhemispheric synchrony from 40 weeks of CA. Five EEG states can be distinguished: wakefulness, active sleep (two patterns) and quiet sleep (two patterns) states (see Appendix):

Wakefulness: Activité moyenne

Active sleep (REM sleep):

- Mixed activity: at the beginning of the sleep cycle
- Low-voltage irregular (LVI): low-voltage irregular pattern after a quiet sleep state

Quite sleep state (NREM sleep):

- Tracé alternant (TA)—alternating tracing, intermittent pattern
- High-voltage slow (HVS)—high-voltage slow pattern:

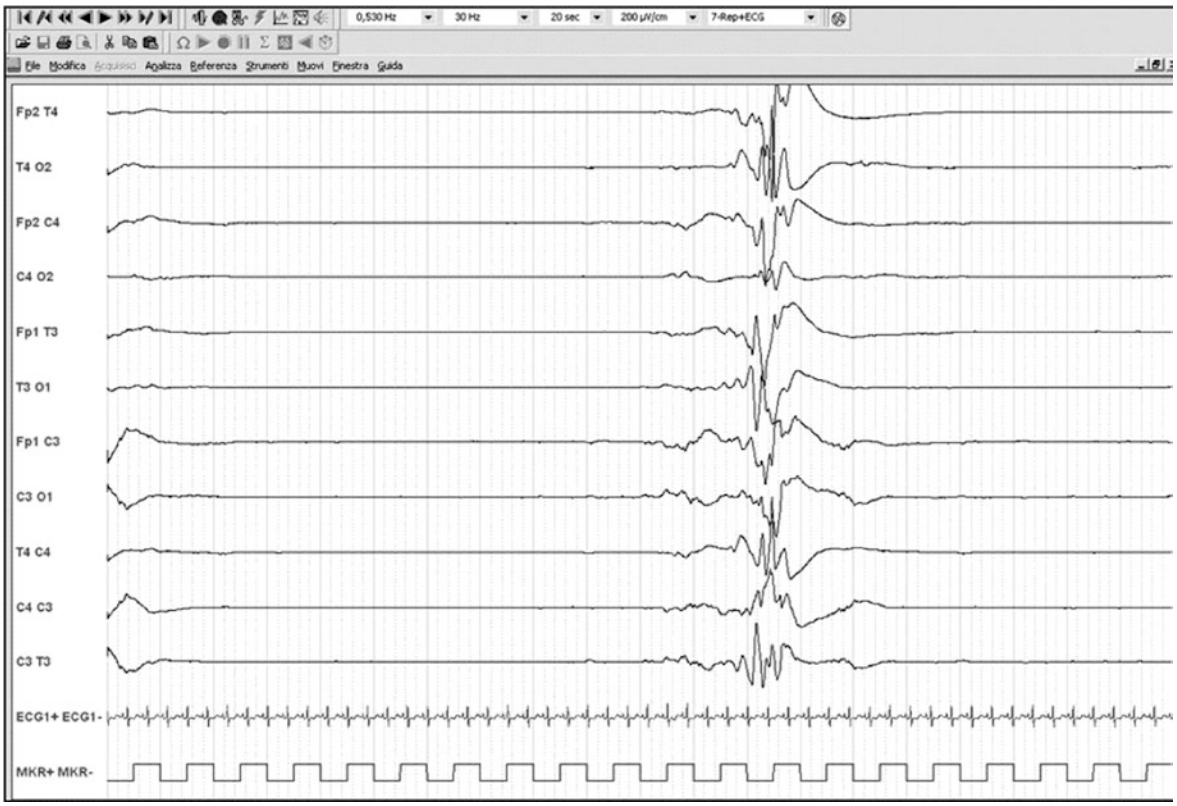

Fig. 11.1 24 weeks GA, 24.4 weeks CA. Discontinuous tracing with electrical quiescence. Bilateral synchronous 3–4 s burst with sharp theta activity (4–5 Hz, 50–350 µV), predominant over temporal regions. An isolated diffuse delta wave (up to 350 µV) is intermingled or follows immediately the burst. This newborn (the same in Figs. 11.1, 11.2, 11.3, and 11.4) was mechanically ventilated for non-neurological reasons. Spontaneous motility and cerebral ultrasound were normal. The inter-bursts interval is CA dependent and has its longest duration at this age

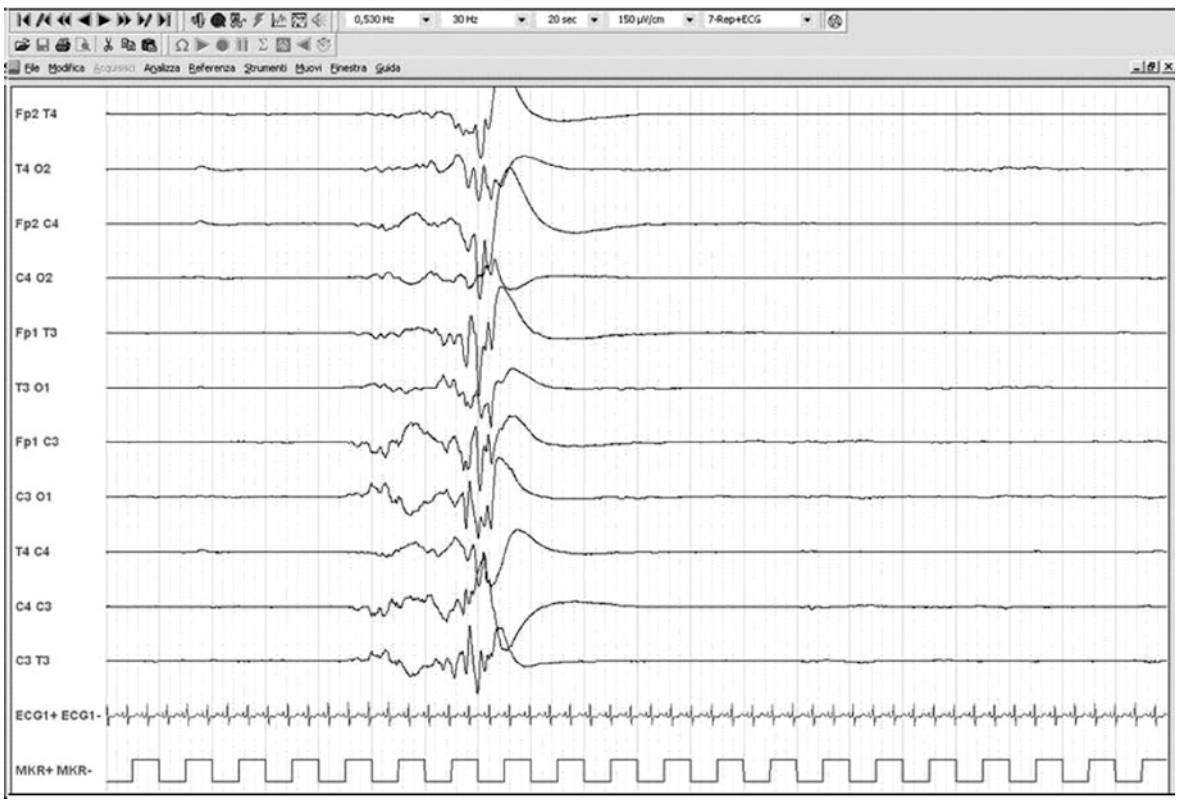

Fig. 11.2 24 weeks GA, 24.4 weeks CA. Discontinuous tracing with electrical quiescence. Synchronous bilateral burst in a discontinuous tracing. Notice that the activity in the burst is not symmetrical

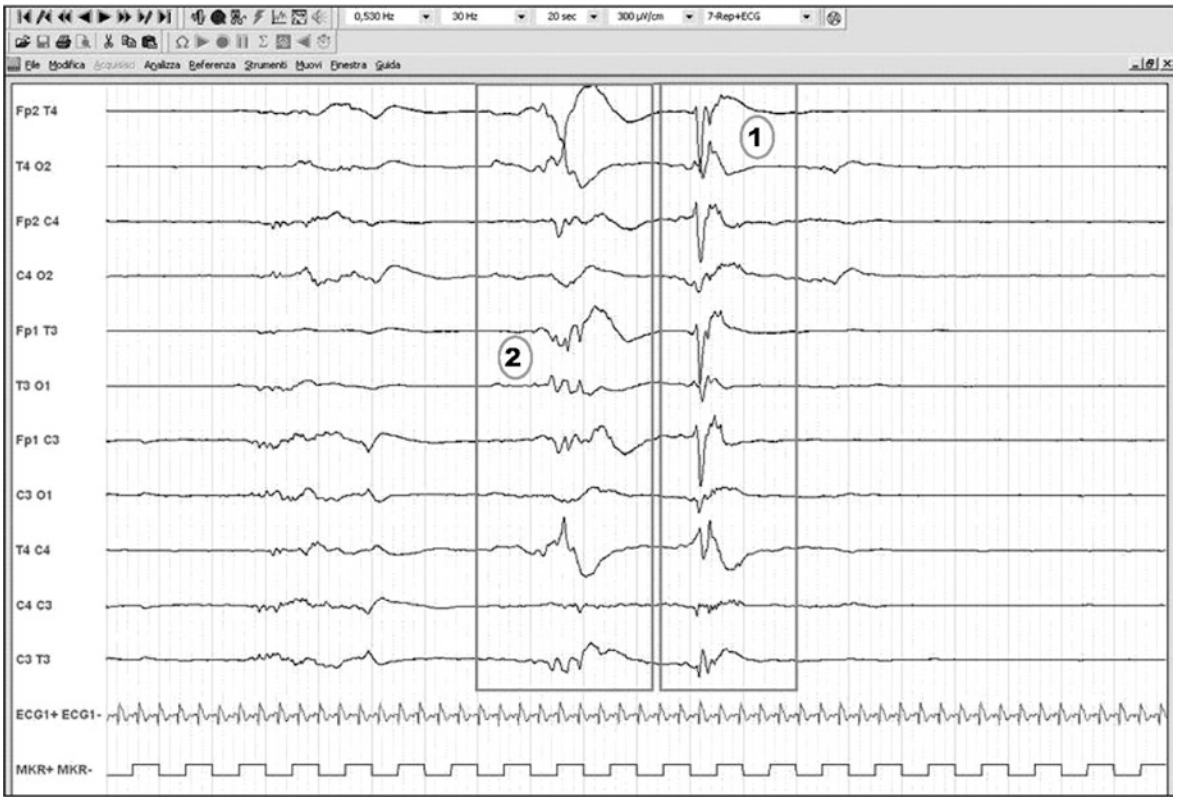

Fig. 11.3 24 weeks GA, 25.2 weeks CA. Discontinuous tracing with electrical quiescence. Notice in the burst (*1*) sharp and dysphasic frontal slow waves (negative-positive course up to 400 μV), (*2*) temporal theta activity (up to 120 μV), associated with a diffuse delta wave of high amplitude (up to 350 μV), predominately over temporal regions. The electrical quiescence periods decrease progressively

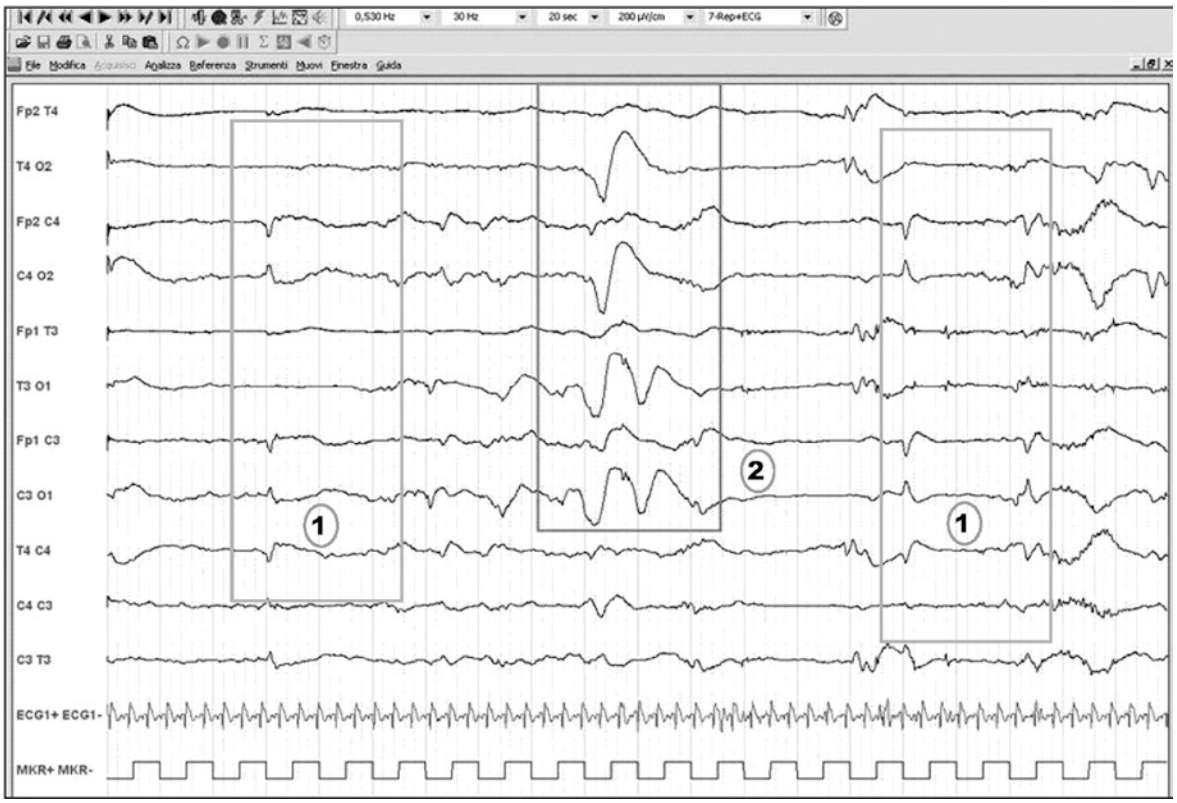

Fig. 11.4 24 weeks GA, 25.2 weeks CA. Discontinuous tracing: (*1*) period of more continuous and diffuse low-voltage activity (less than 150 μV). (*2*) Bilateral delta activity over occipital regions up to 400 μV, isolated or in short sequences

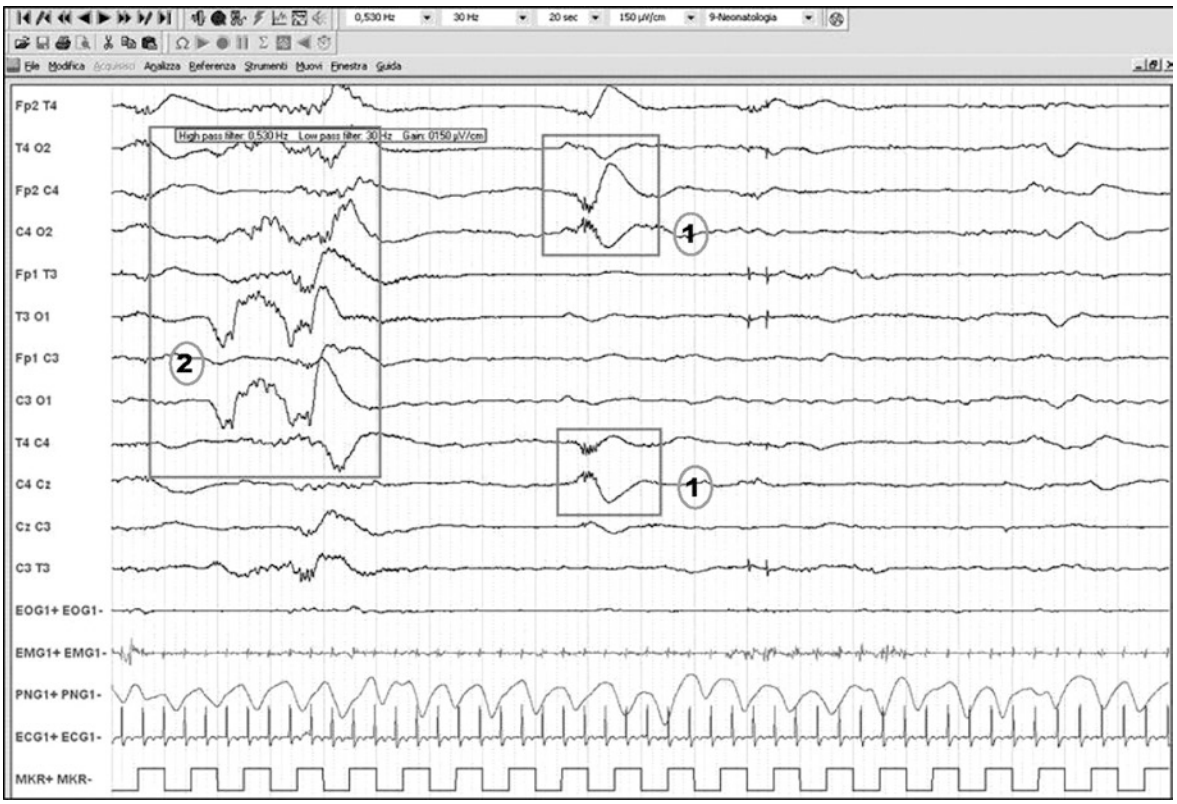

Fig. 11.5 27 weeks GA, 29–30 weeks CA. Discontinuous tracing: (*1*) Rolandic and (*2*) occipital delta brushes (delta wave with superimposed beta complexes): the amplitude of the slow wave is between 150 and 300 μV, while beta activity is generally less than 40 μV

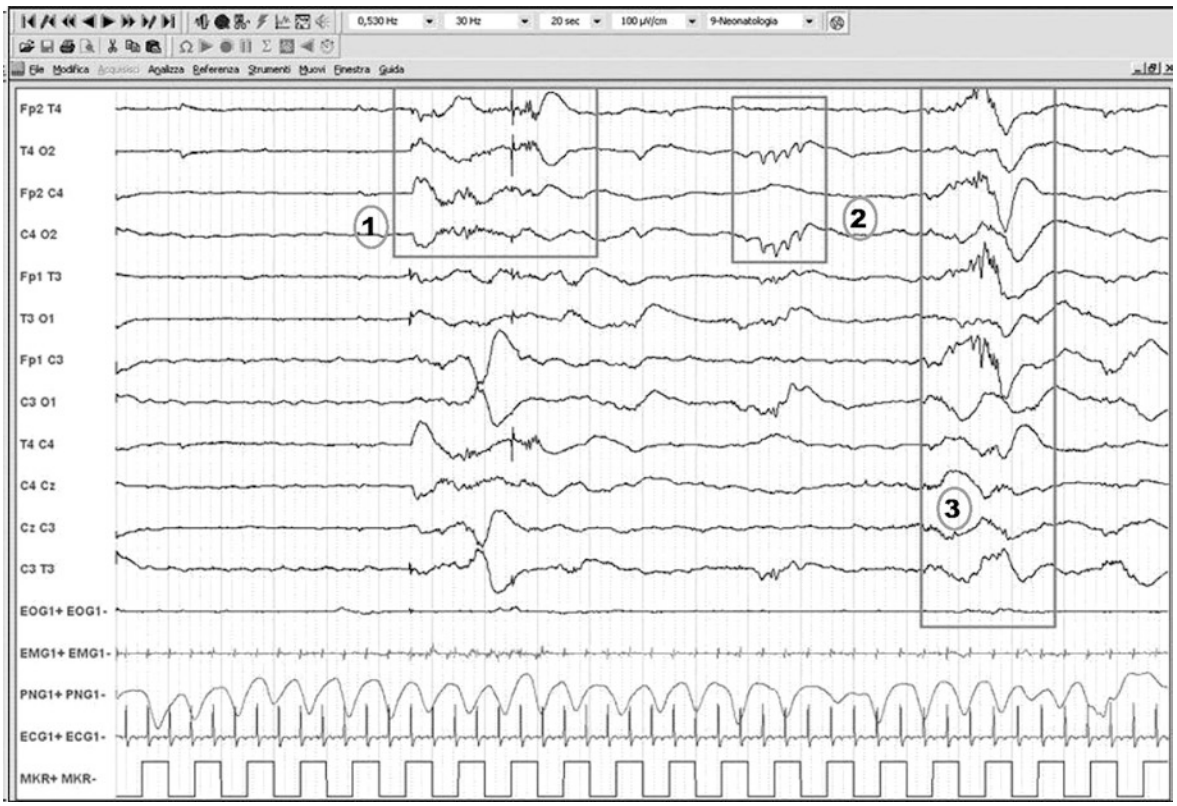

Fig. 11.6 27 weeks GA, 29–30 weeks CA. Discontinuous tracing: (*1*) Rolandic and occipital delta brushes (delta wave amplitude is less than 100 μV); (*2*) occipital rhythmic theta activity (less than 70 μV) in the right side; (*3*) notice in the bursts a diffuse delta activity

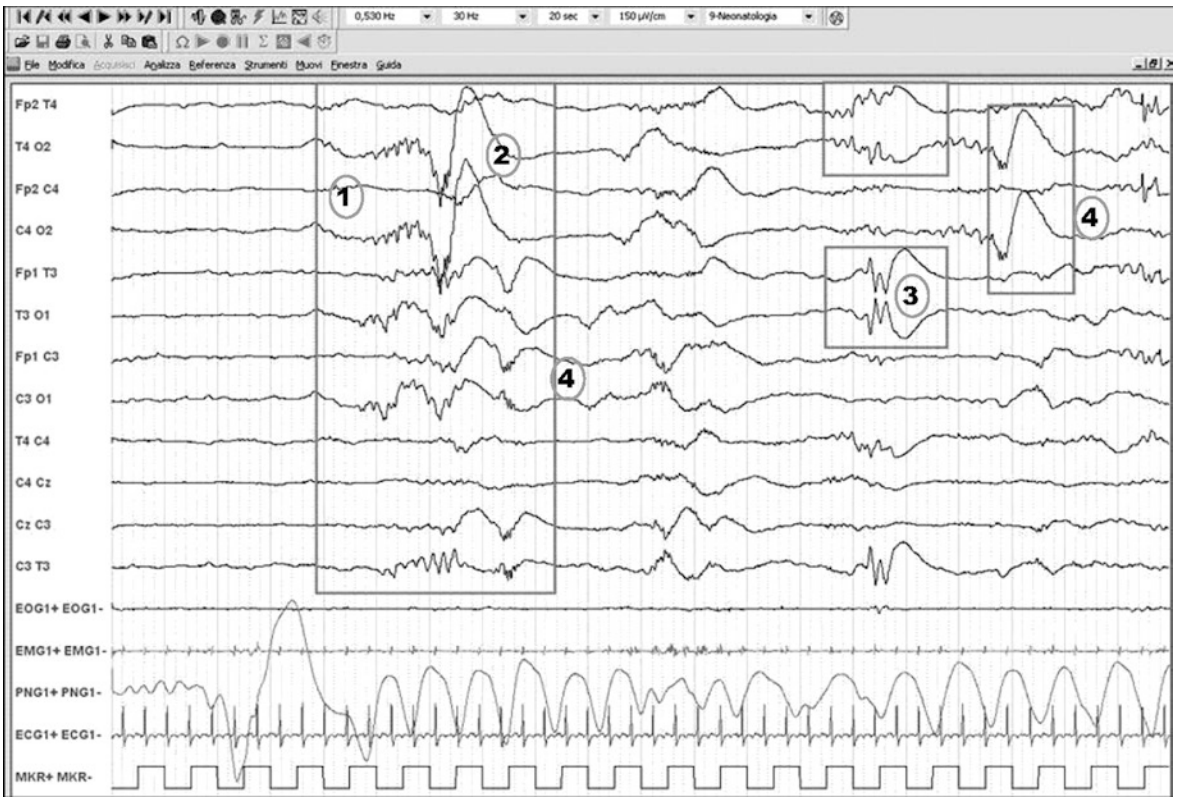

Fig. 11.7 27 weeks GA, 29–30 weeks CA. Discontinuous tracing: notice a 20 s epoch with continuous activity related to active sleep. (*1*) rhythmic theta occipital activity; (*2*) bilateral occipital delta activity (up to 400 μV); (*3*) sharp and bilateral temporal theta (up to 150 μV); (*4*) Rolandic and occipital delta brushes (delta wave amplitude between 150 and 300 μV)

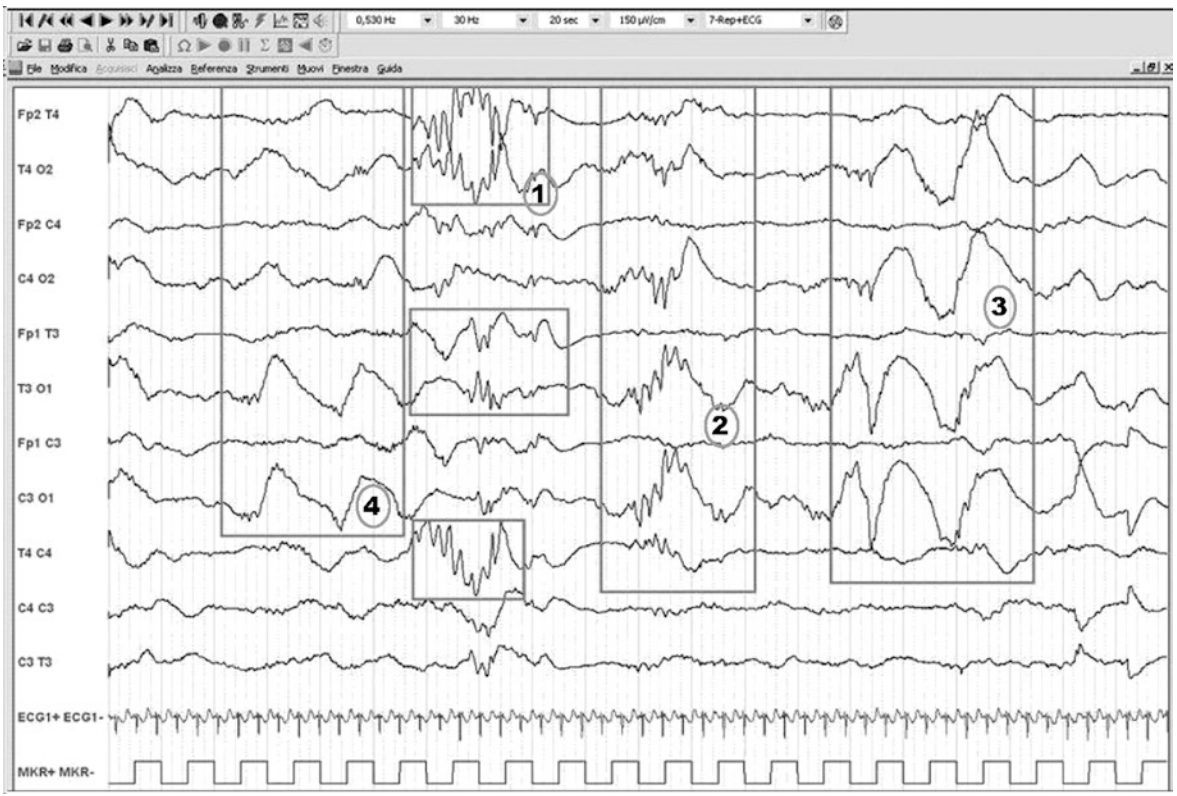

Fig. 11.8 24 weeks GA, 29–30 weeks CA. In a discontinuous tracing epochs lasting 20 s with continuous electrical activity consistent with active sleep. Electrical pattern overlapping the description in Fig. 11.7 (same CA, different GA in the two newborns): (*1*) bilateral sharp theta temporal activity for 2 s; (*2*) bilateral occipital theta rhythmic activity; (*3*) occipital rhythmic delta wave, bilateral and synchronous; (*4*) occipital delta brushes

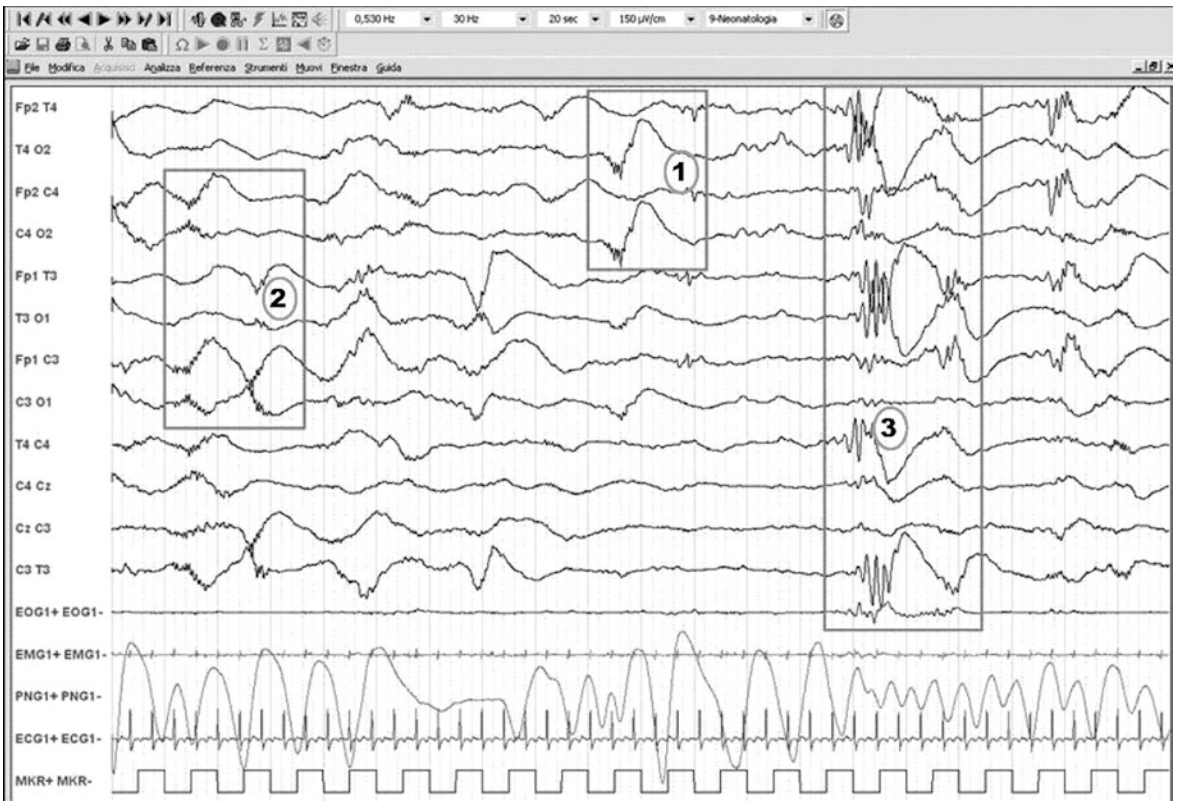

Fig. 11.9 27 weeks GA, 29–30 weeks CA. In a discontinuous tracing epochs lasting 20 s with continuous electrical activity consistent with active sleep: delta brushes (*1*) occipital and (*2*) Rolandic; (*3*) sharp and rhythmic bilateral temporal theta activity

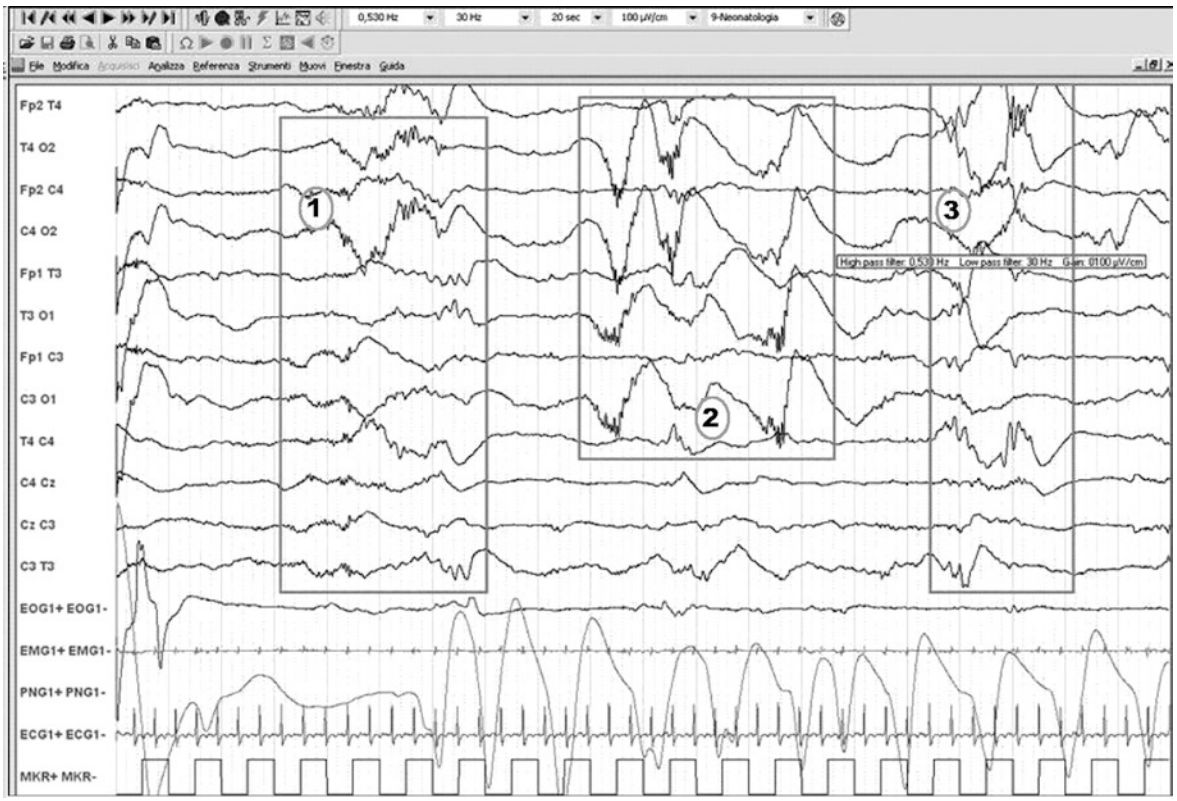

Fig. 11.10 27 weeks GA, 29–30 weeks CA. Discontinuous tracing: (*1*) Low-voltage alpha activity over right occipital and left central regions; (*2*) bilateral and synchronous delta brushes over occipital regions; (*3*) sharp rhythmic theta activity over right temporal region. Between the three patterns described there are brief (1–2 s-long) with quiescent activity. This condition is related to active sleep

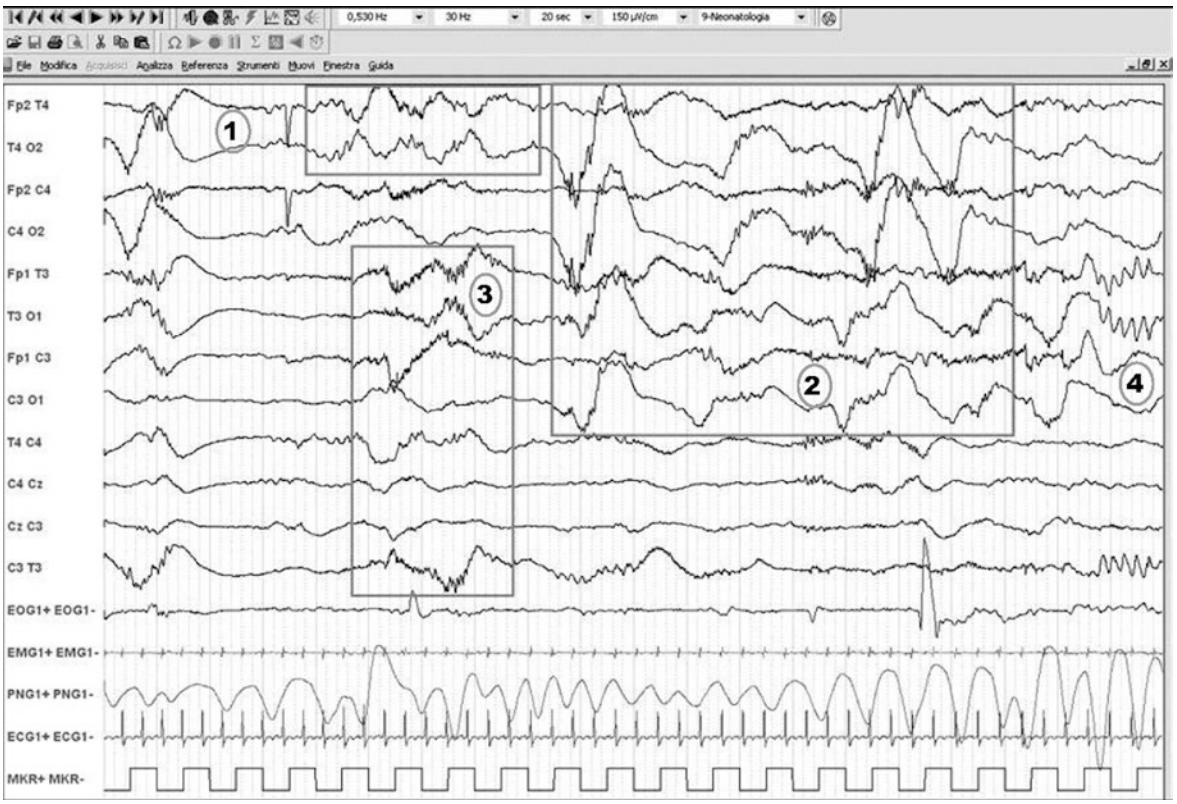

Fig. 11.11 27 weeks GA, 29–30 weeks CA. Transition from active to quiet sleep: (*1*) temporal alpha activity; (*2*) bilateral occipital delta activity (up to 300 μV); (*3*) occipital and Rolandic delta brushes; (*4*) 2 s theta rhythmic activity over left temporal region

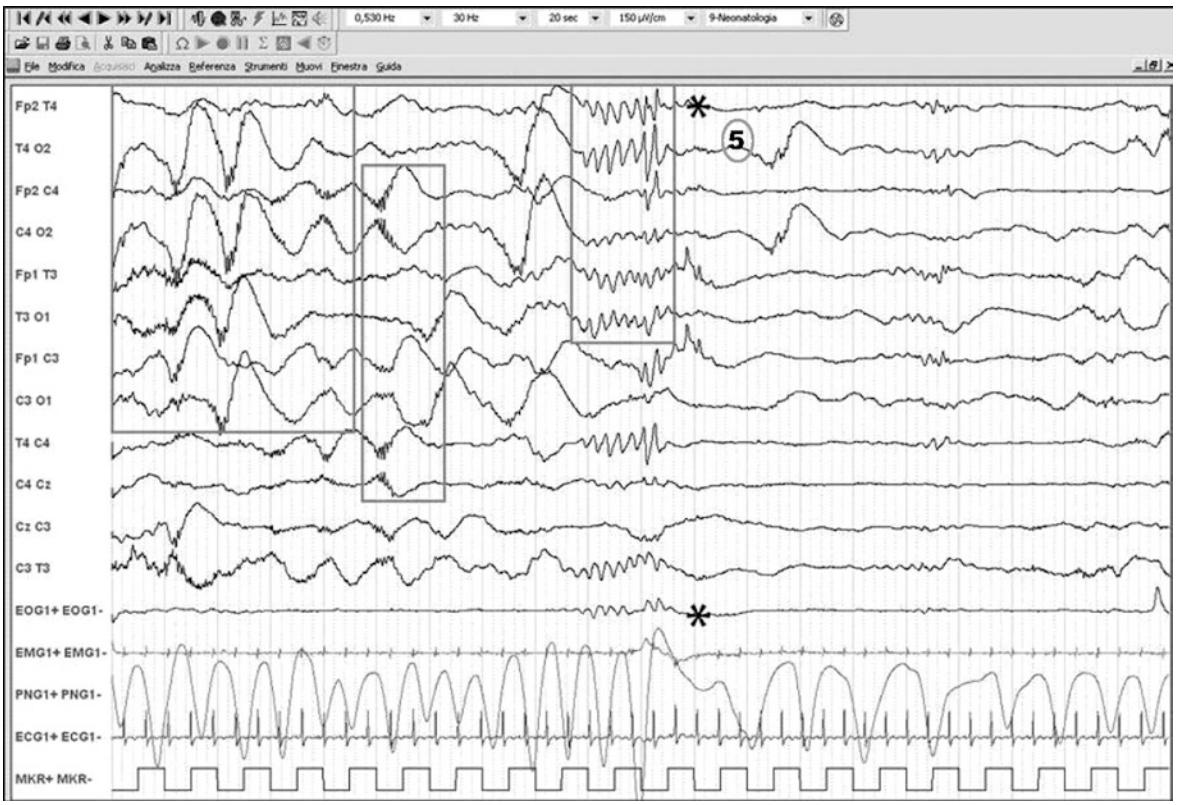

Fig. 11.12 27 weeks GA, 29–30 weeks CA. Same patient of Fig. 11.11 with overlapping features. Moreover (*5*) transition pattern to discontinuous tracing

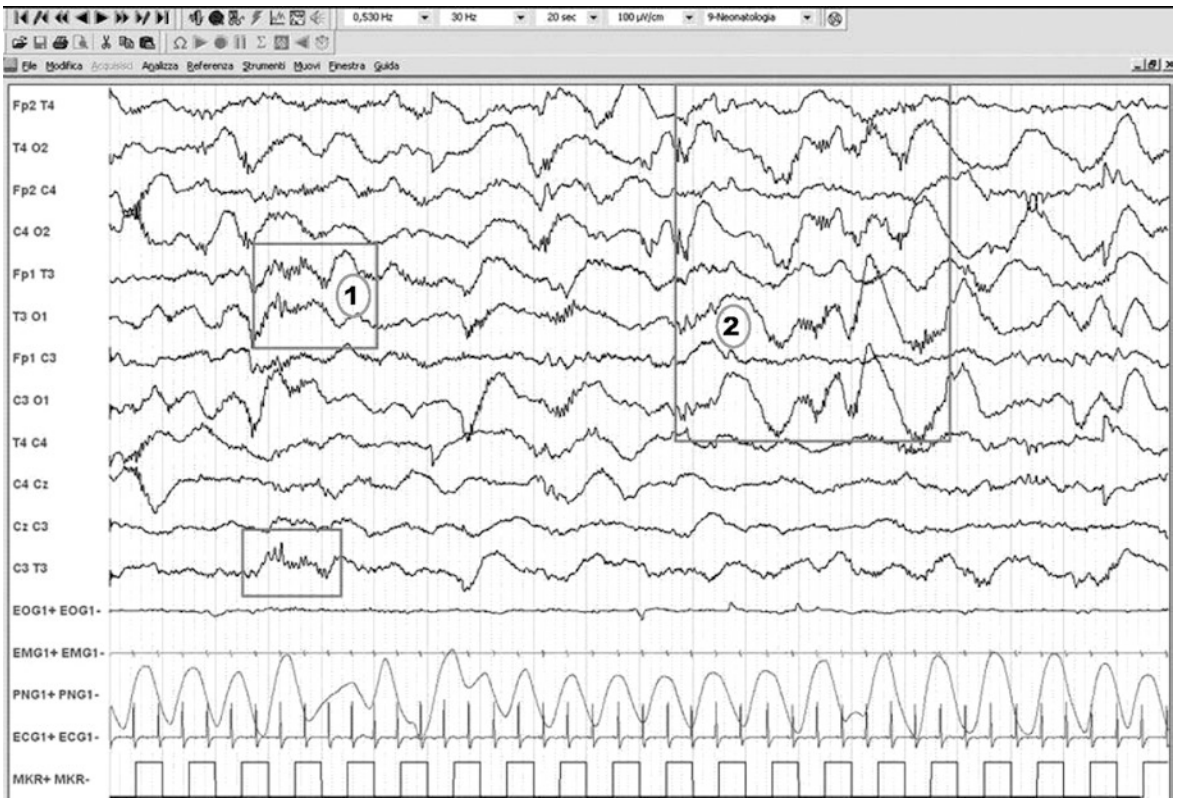

Fig. 11.13 27 weeks GA, 33–34 weeks CA. Continuous electrical activity in REM/active sleep: (*1*) slow amplitude temporal rhythmic alpha activity; (*2*) sequence of delta brushes over bilateral occipital regions

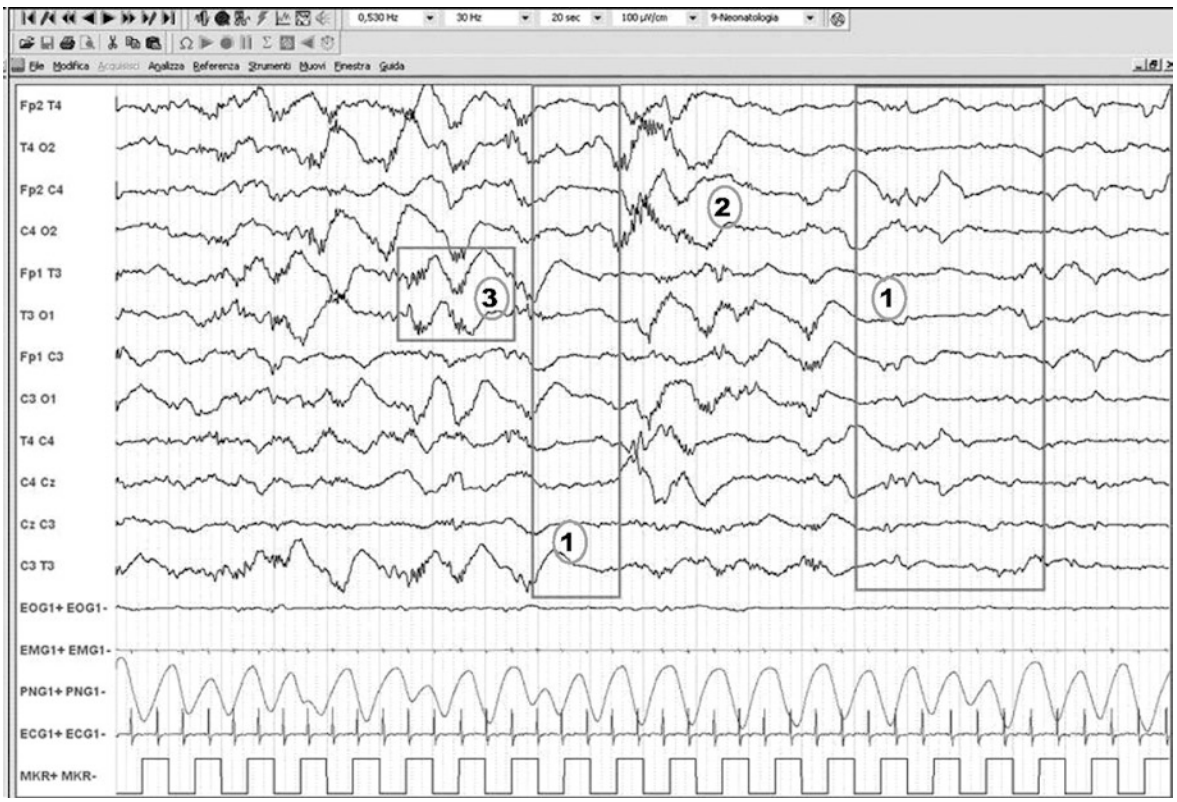

Fig. 11.14 27 weeks GA, 33–34 weeks CA. NREM/Quiet sleep. The pattern is still discontinuous, but (*1*) interbursts of inactivity are progressively reduced in duration comparing to previous CA; (*2*) bilateral delta activity over occipital regions; (3) temporal and occipital delta brushes

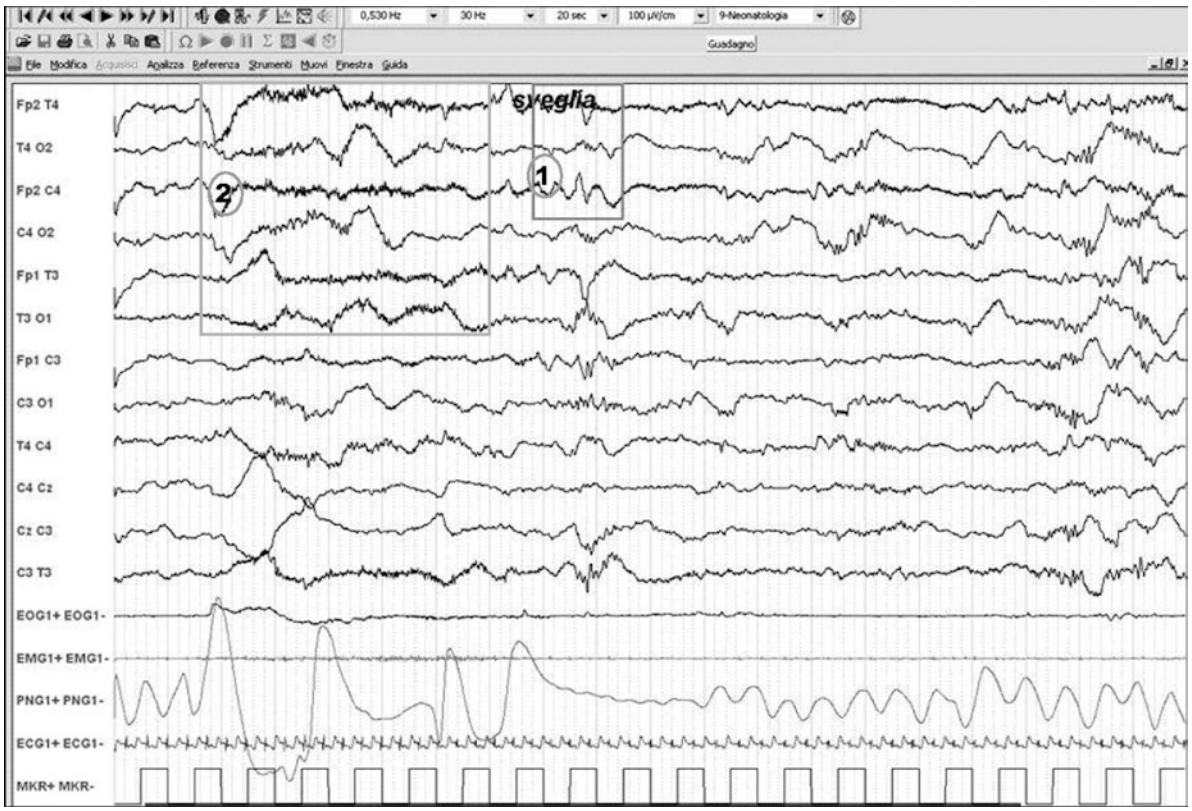

Fig. 11.15 32 weeks GA, 35–36 weeks CA. Quiet alert: diffuse continuous electrical activity, mostly theta (less than 60 μV), several delta and alpha waves (sveglia = awake). (*1*) Anterior sleep frontal transients over the right side; (*2*) artifactual fast activity (muscles) in the frontal right leads and temporal left region related to a global movement documented by the artifact of pneumogram polygraphic channel

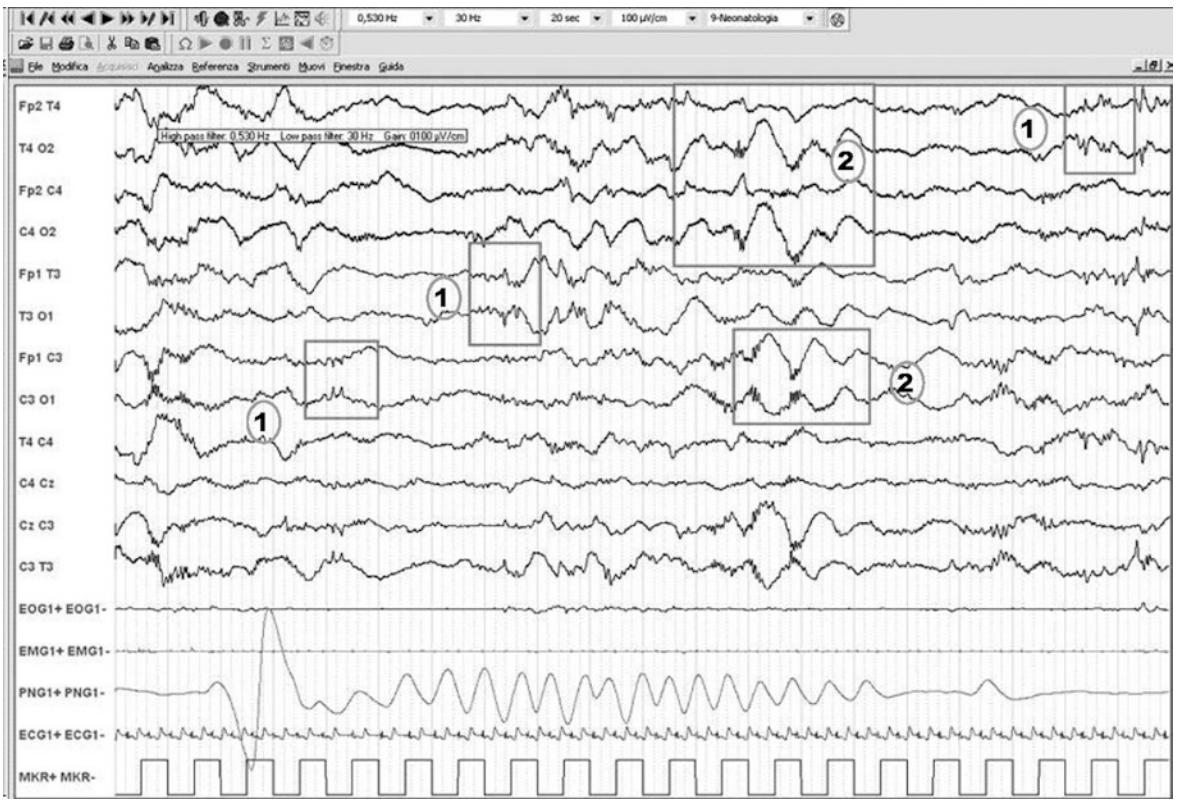

Fig. 11.16 32 weeks GA, 35–36 weeks CA. Continuous electrical activity in transitional sleep pattern. (*1*) Multifocal and isolated slow spikes over central and temporal left regions; (*2*) delta brushes over right occipital and left central regions

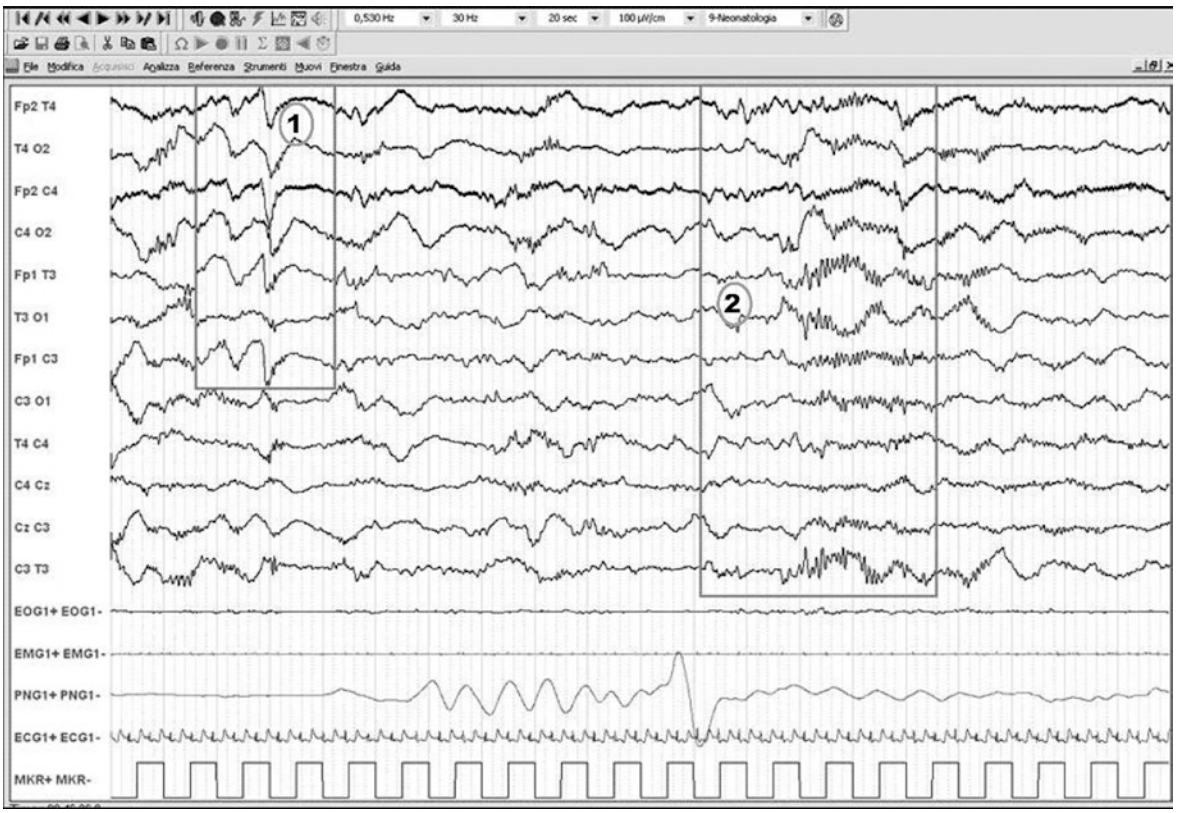

Fig. 11.17 32 weeks GA, 35–36 weeks CA. Active sleep: continuous diffuse theta-delta activity. (*1*) Bilateral frontal sharp transients (*encoche frontale, Dreyfus-Brisac, 1962)*; (*2*) bilateral central and temporal alpha-beta activity. Irregular activity in the PNG polygraphic channel

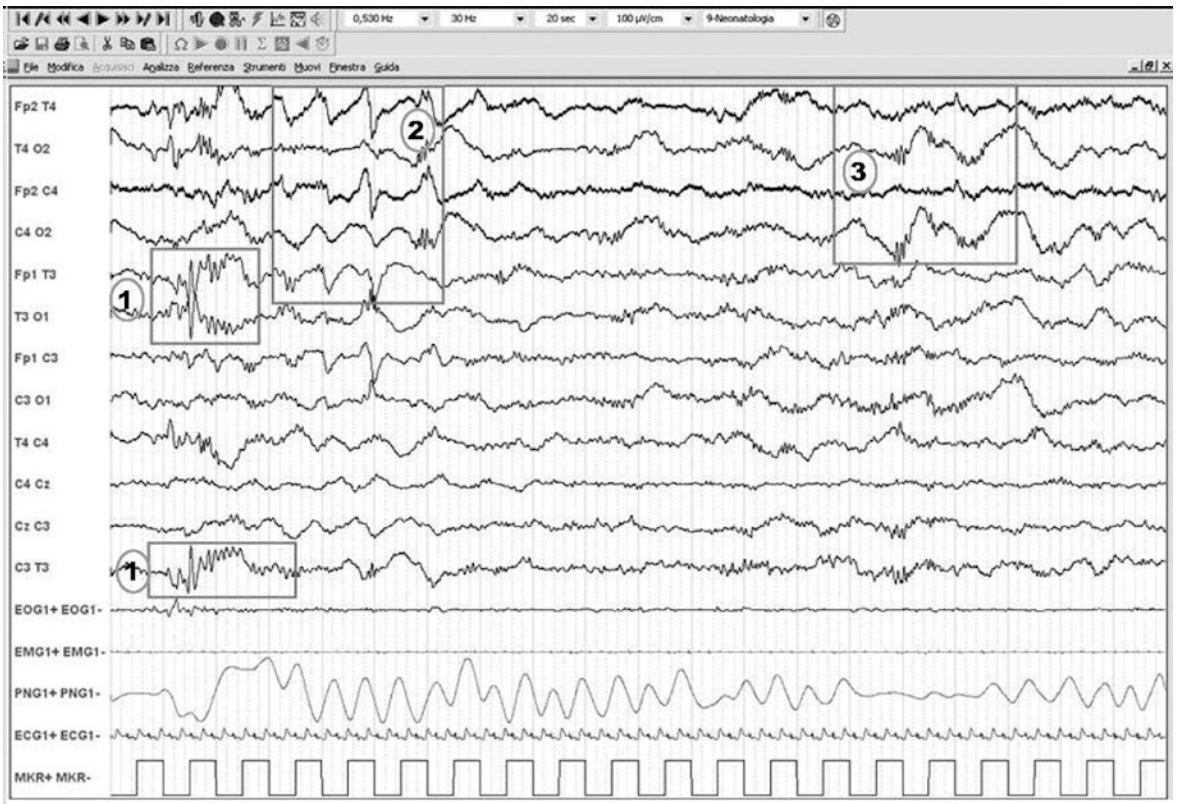

Fig. 11.18 32 weeks GA, 35–36 weeks CA. Active sleep: continuous background activity with (*1*) left theta-alpha activity associated with temporal medium voltage isolated sharp wave; (*2*) rhythmic bifrontal delta activity associated with frontal sharp transients; (*3*) occipital delta brushes over the right side

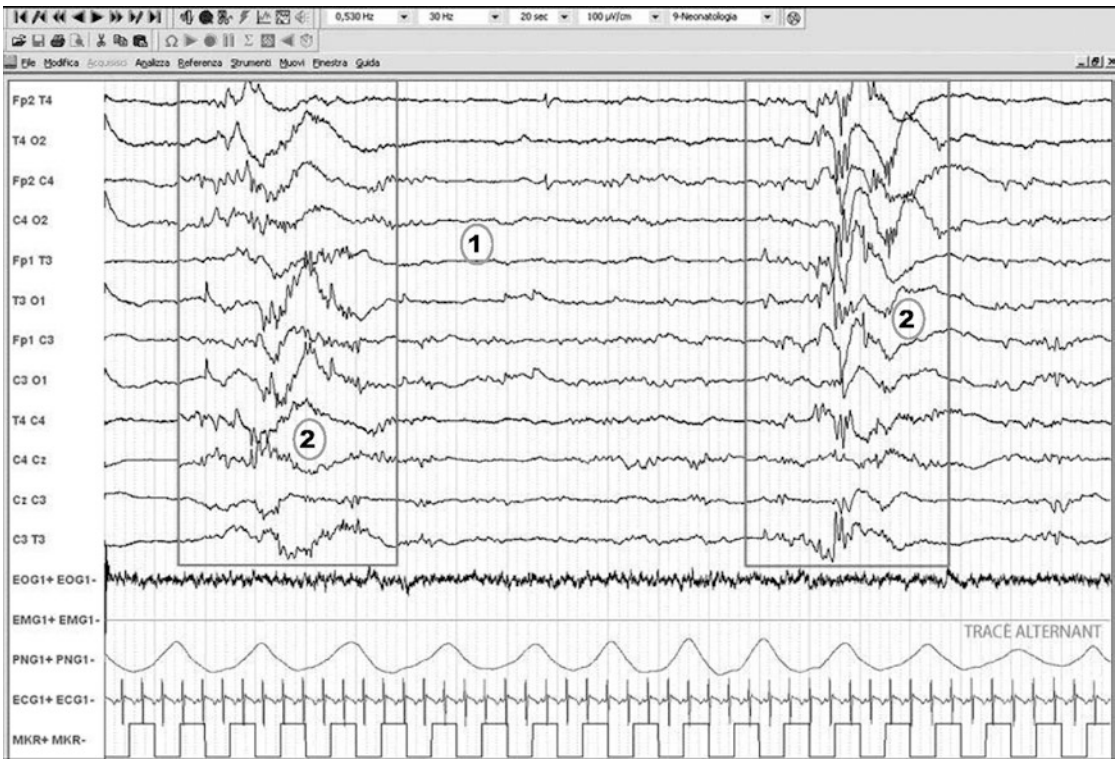

Fig. 11.19 33 weeks GA, 37–38 weeks CA. *Tracé alternant* pattern in deep non-rapid eye movement (NREM/quiet) sleep: (*1*) periods (8–10 s) of discontinuity with low-voltage (less than 50 μV) theta activity; (*2*) bilateral bursts (3–5 s) with theta (50–100 μV) and delta (up to 300 μV) activity with intermingled low-voltage beta activity. Concordance of polygraphic parameters: absent ocular movements; regular breathing and heart rate frequency

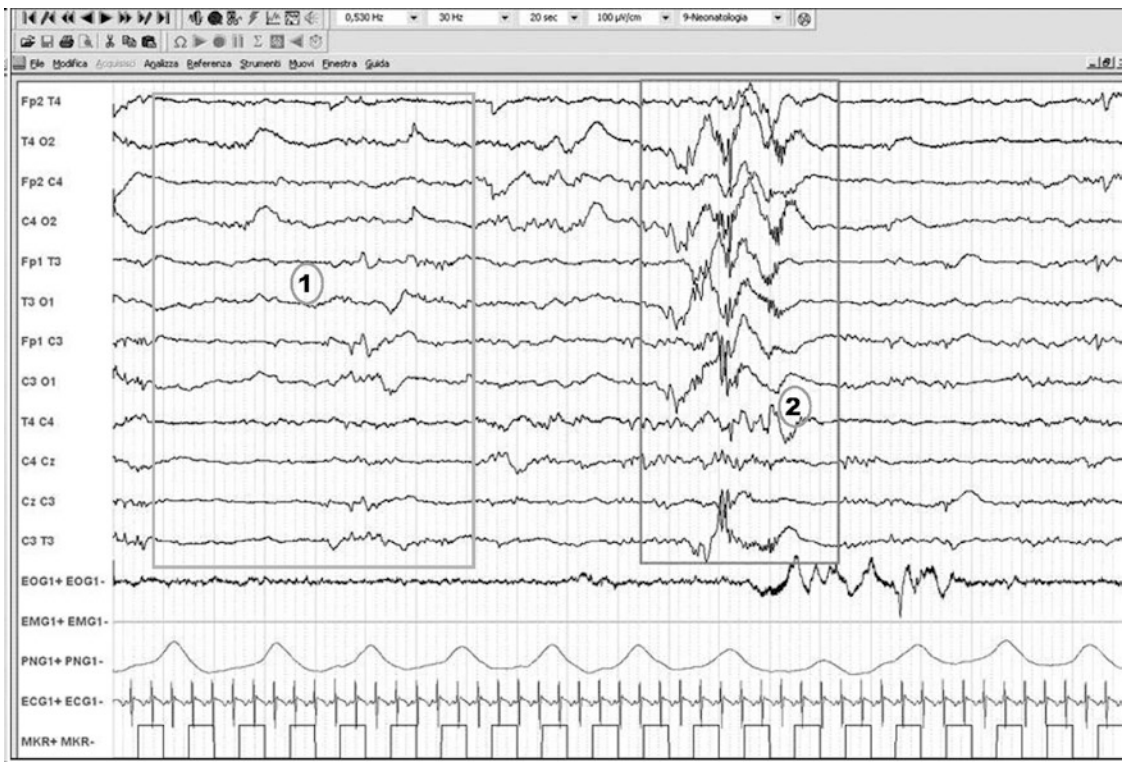

Fig. 11.20 33 weeks GA, 37–38 weeks CA. *Tracé alternant* pattern in deep non-rapid eye movement (NREM/quiet) sleep: (*1*) periods (8–10 s) of discontinuity with low-voltage (less than 50 μV) theta activity; (*2*) bilateral bursts (3–5 s) with theta (50–100 μV) and delta (up to 300 μV) activity with intermingled low-voltage beta activity. Concordance of polygraphic parameters: in the EOG channel artifacts related to abnormal electrode contact; regular breathing and heart rate frequency

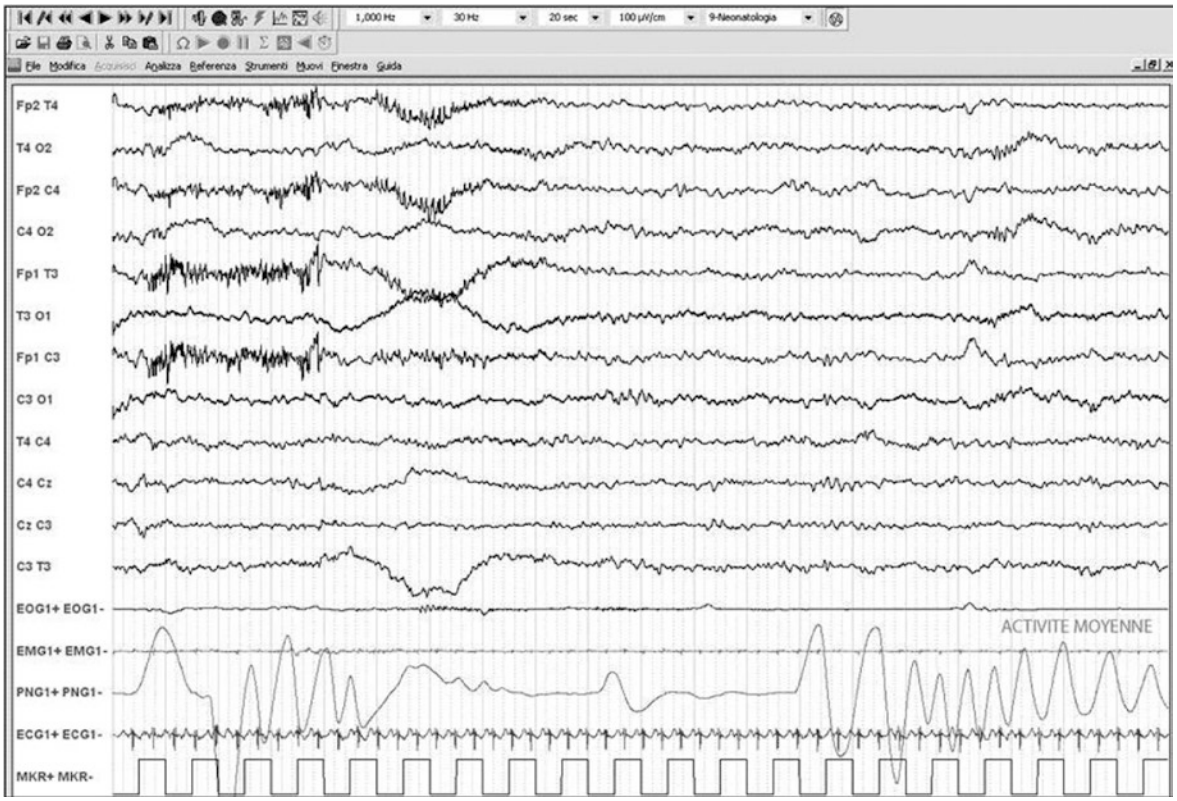

Fig. 11.21 29 weeks GA, 37–38 weeks CA. A*ctivité moyenne* pattern: in quiet awake state with open eyes, continuous diffuse theta (4–6 Hz, 40–60 μV) activity. Medium voltage EMG activity in anterior leads. Polygraphic parameters: in the EOG rapid eyes movements; irregular breathing and increasing heart rate frequency

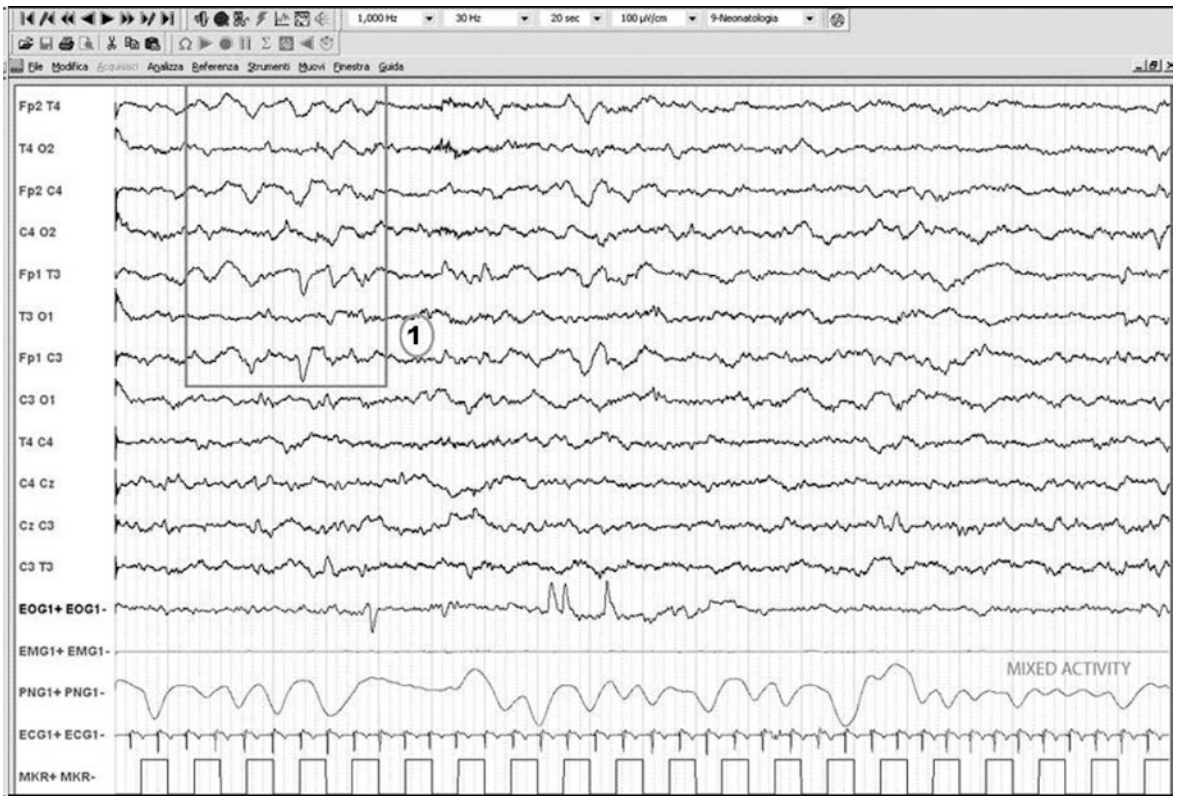

Fig. 11.22 38 weeks GA, 39 weeks CA. Active sleep before quiet sleep: continuous diffuse theta (4–6 Hz, 40–60 μV) activity with superimposed diffuse slow delta activity; (*1*) rhythmic bifrontal delta activity and frontal sharp transients on the left side

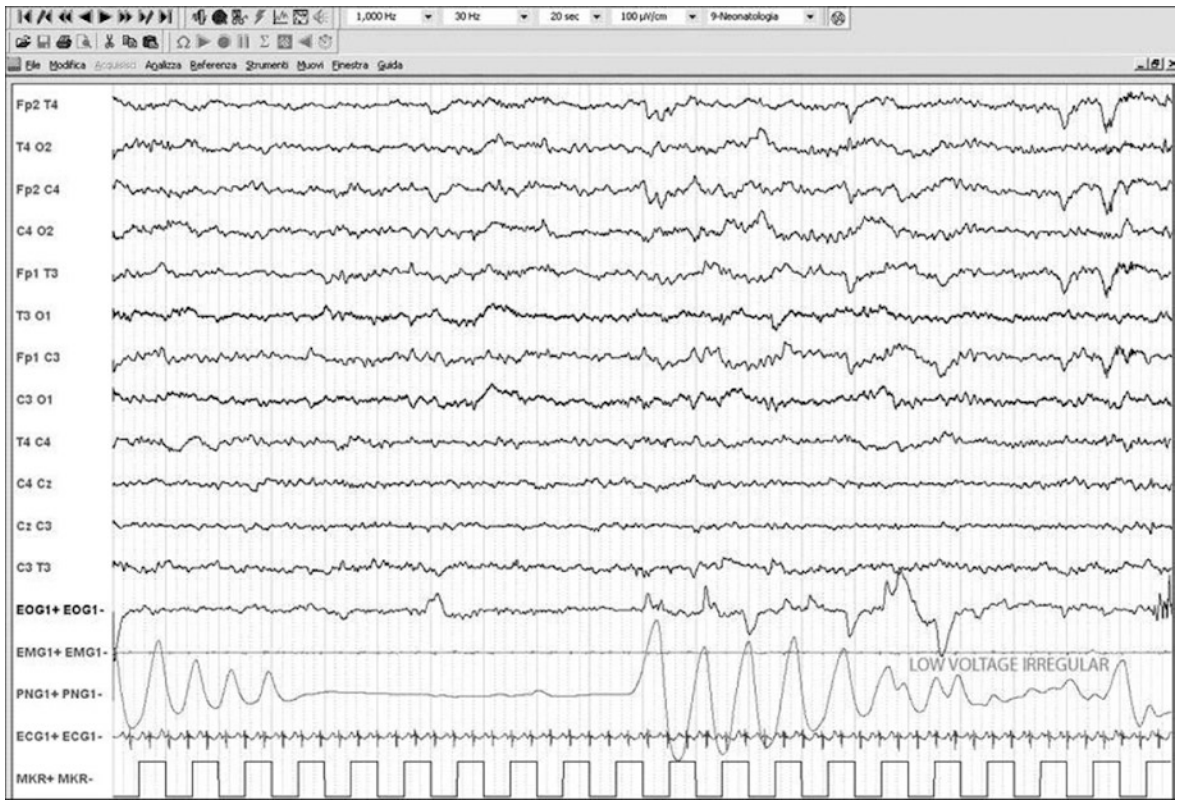

Fig 11.23 29 weeks GA, 38 weeks CA. Low-voltage irregular pattern: REM/active sleep after NREM/quiet sleep: mixed diffuse theta (4–6 Hz, 40–60 μV) activity. Polygraphic parameters: in the electrooculogram channel rapid eyes movements, irregular breathing with a 6 s breathing pause

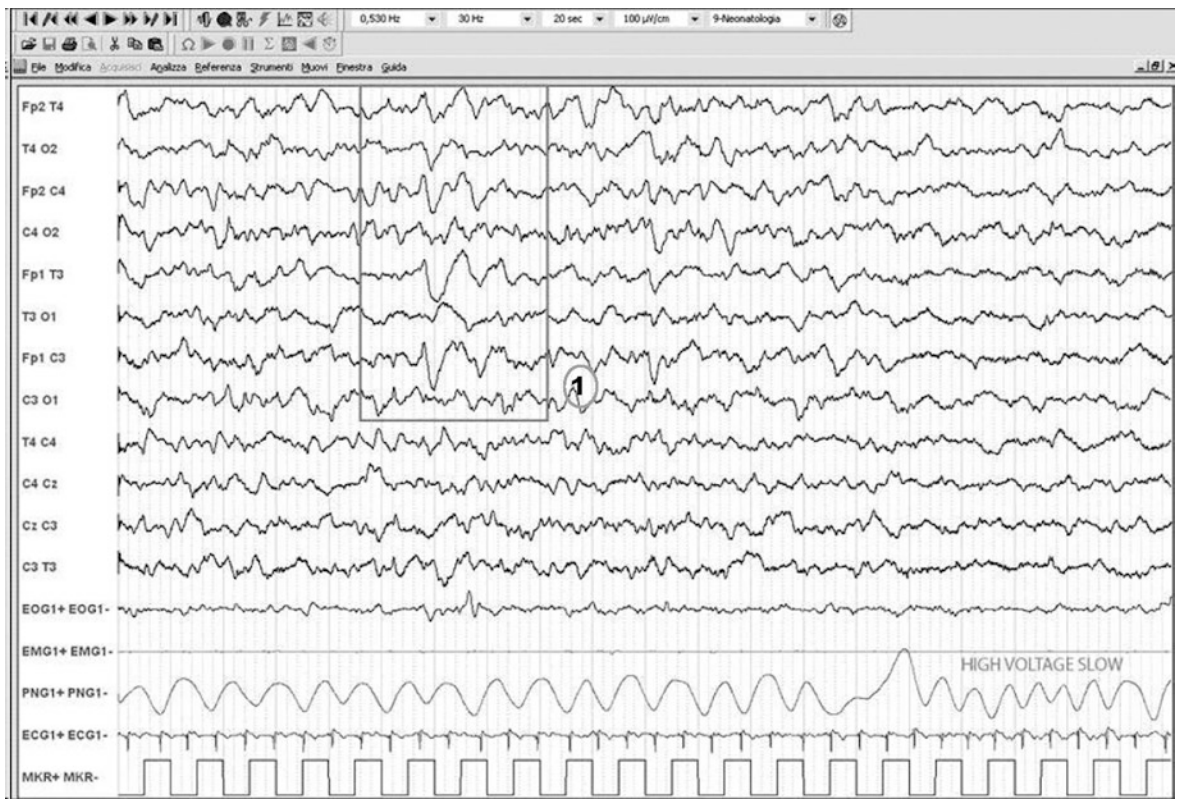

Fig. 11.24 38 weeks GA, 39 weeks CA. High-voltage slow (HVS) pattern: quiet sleep with diffuse and bilateral slow (delta-theta, 0.5–4 Hz, up to 150 μV) activity. (*1*) Rhythmic bifrontal delta activity and frontal sharp transients on the left side

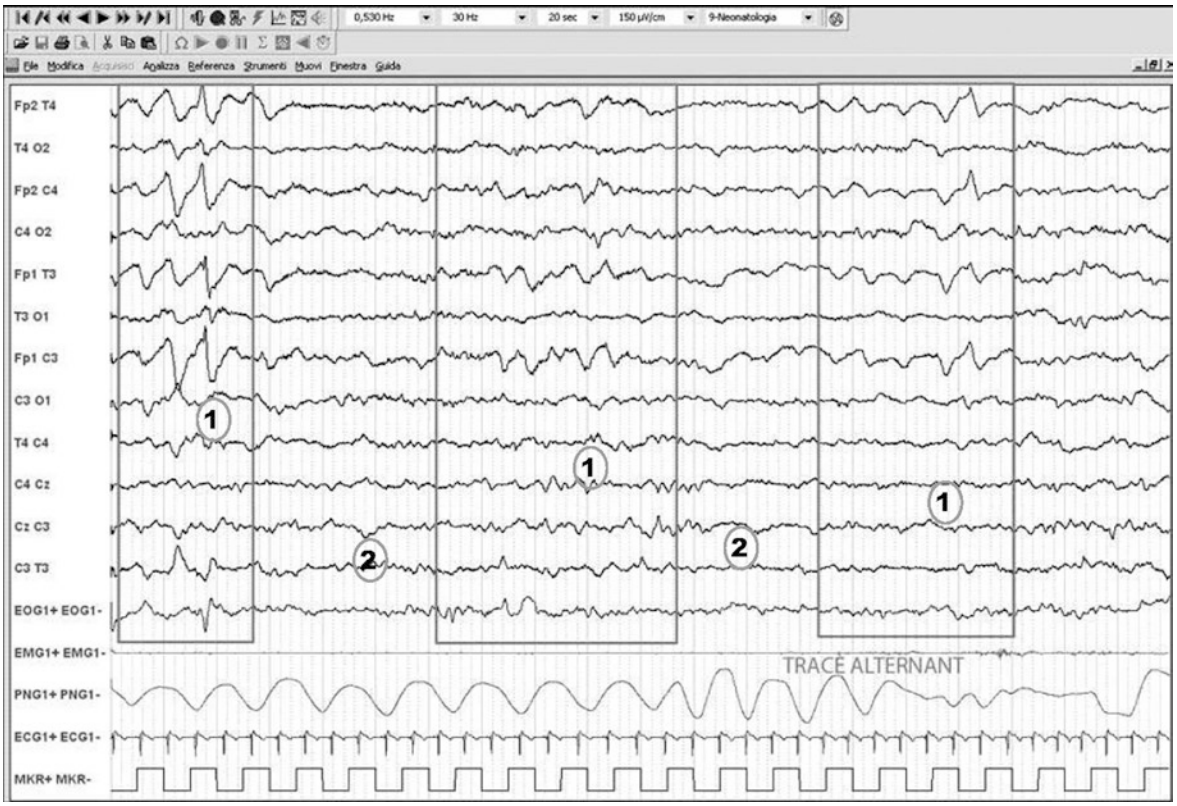

Fig. 11.25 38 weeks GA, 39 weeks CA. *Tracé alternant* pattern during NREM/quiet sleep: (*1*) 2–4 s periods with diffuse delta (up to 100–200 μV) activity intermingled with (*2*) 4–10 s periods with diffuse theta (4–6 Hz, 25–50 μV) activity. Notice within the first burst (*1*): bifrontal rhythmic delta activity with frontal sharp transients

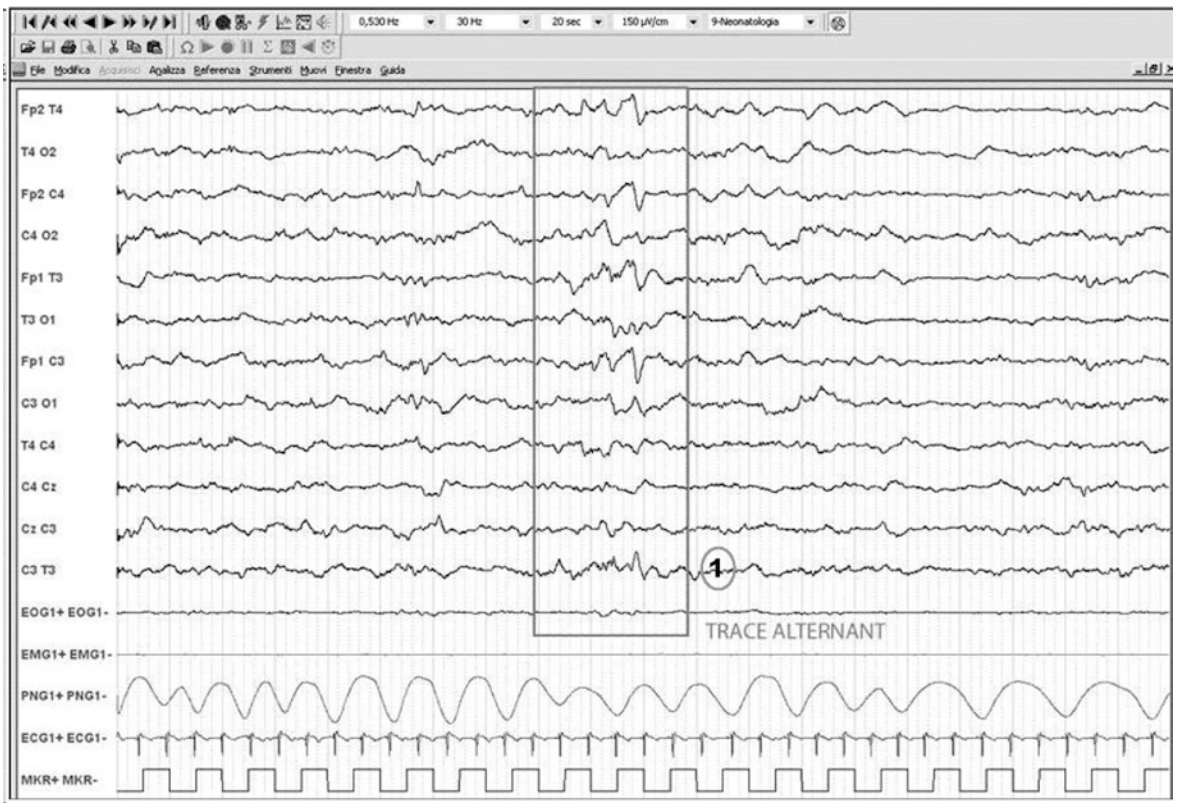

Fig. 11.26 38 weeks GA, 39 weeks CA. *Tracé alternant* pattern evolving to transitional sleep pattern: within 8–10 s periods with diffuse theta (4–6 Hz, 25–60 μV) activity, arise (*1*) a 3–4 s burst with bilateral delta (100–250 μV) activity and frontal sharp transients

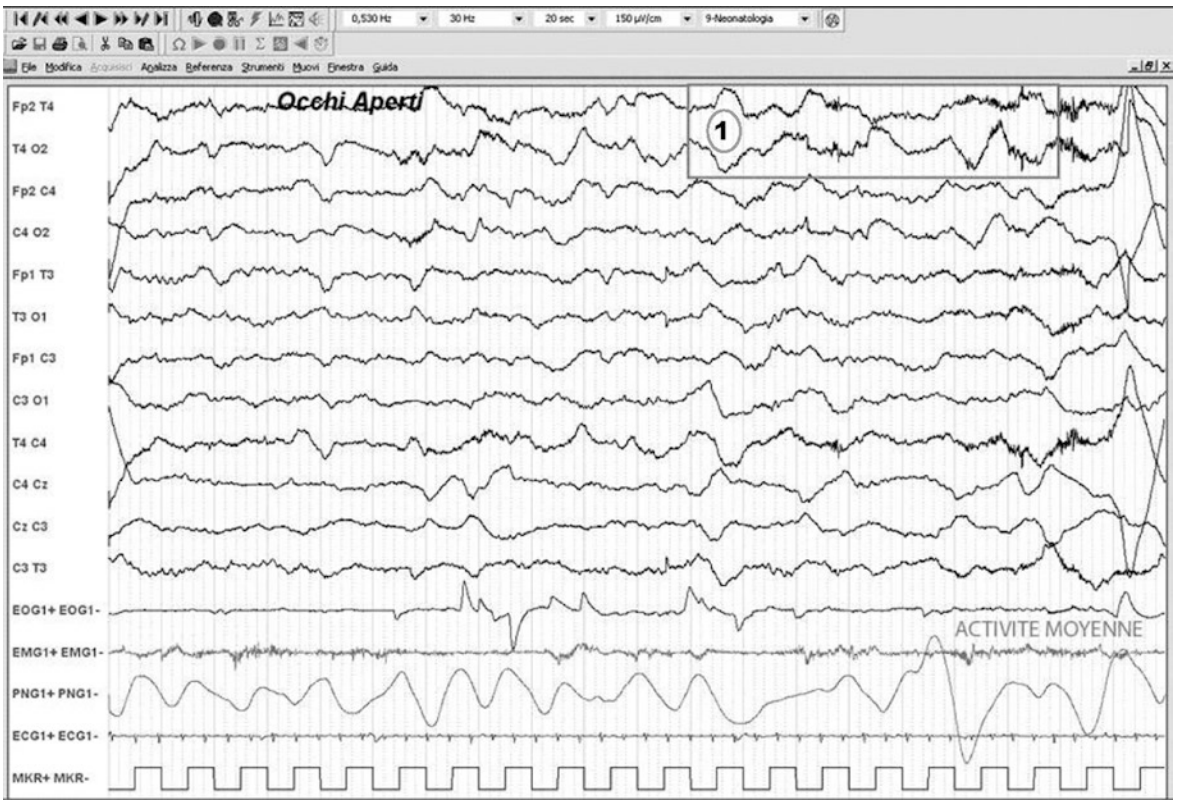

Fig. 11.27 40 weeks GA, 41 weeks CA. A*ctivité moyenne* pattern during awake: within continuous diffuse theta (4–6 Hz, 40–60 μV) activity 1) EMG activity due to sucking bilateral but more evident in the temporal right regions. Polygraphic parameters: according to the awake condition: eyes movements, muscular activity and irregular breathing. (Occhi Aperti = eyes open)

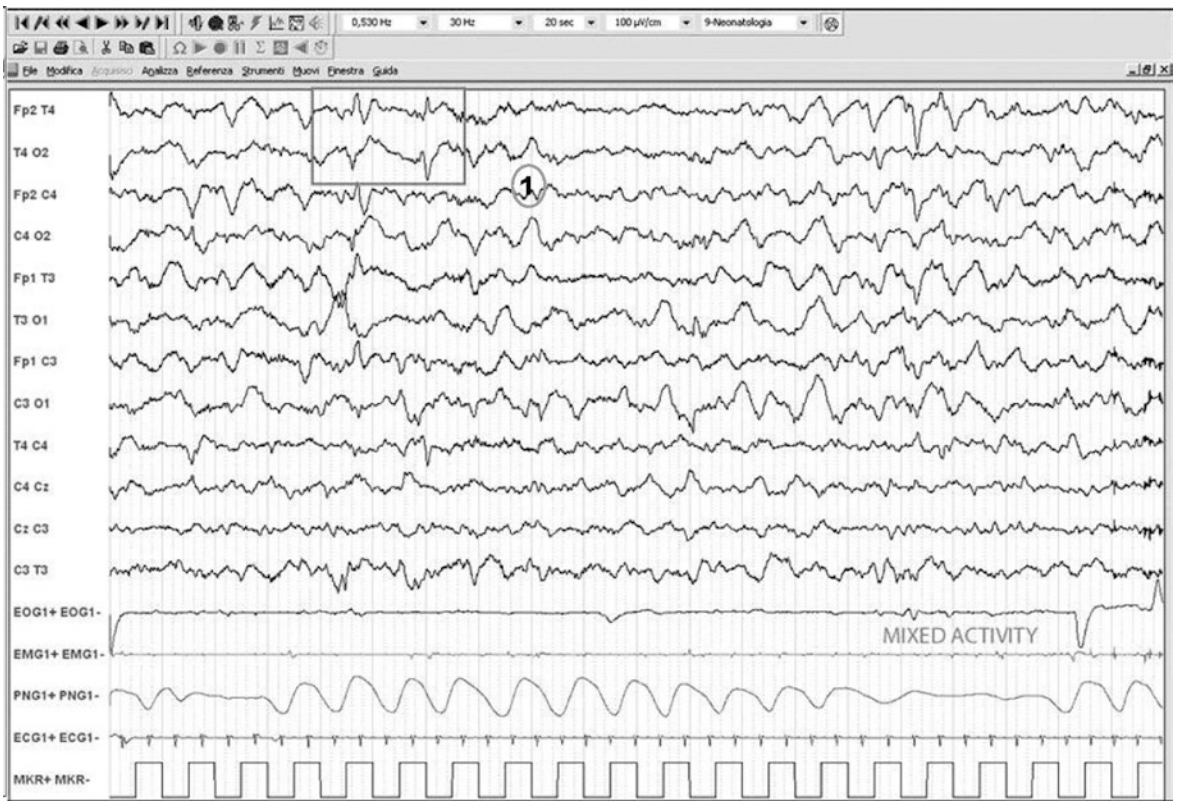

Fig. 11.28 40 weeks GA, 41 weeks CA. Mixed activity pattern before NREM/quiet sleep: prevalence of delta activity compared to theta activity with (*1*) isolated sharp waves in the right temporal region

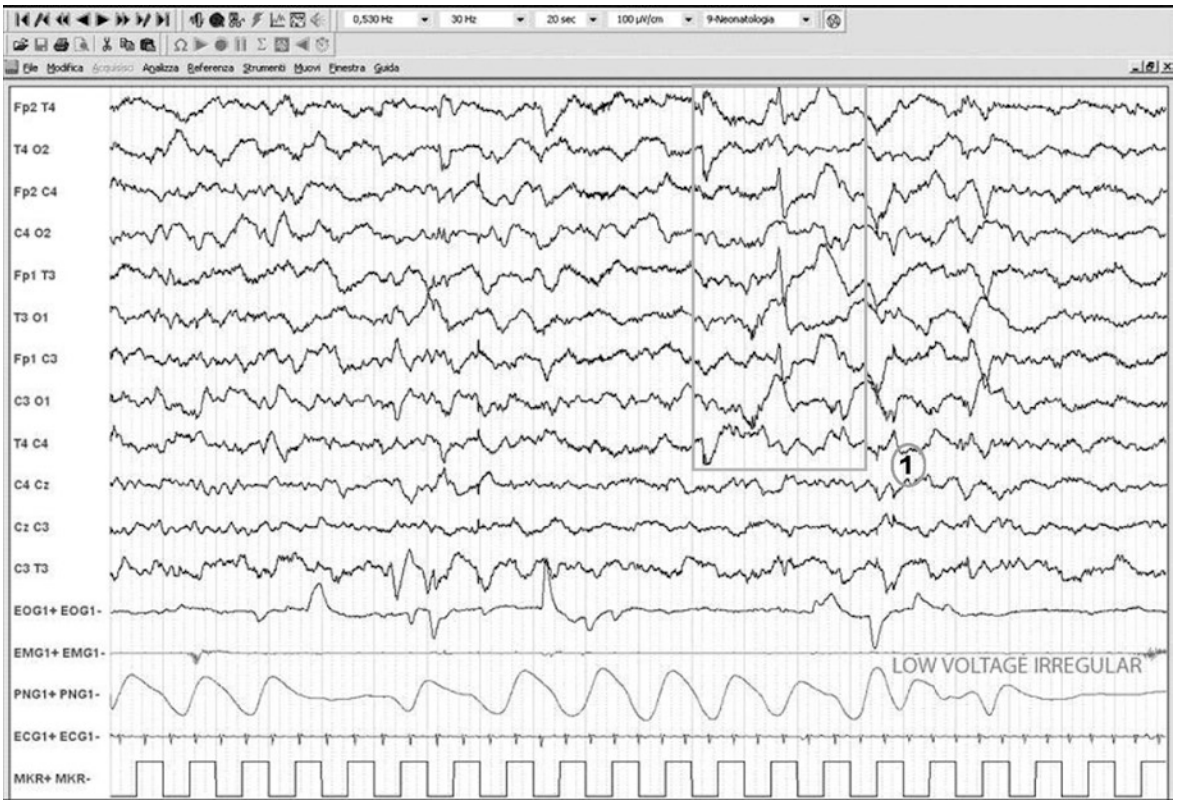

Fig. 11.29 40 weeks GA, 41 weeks CA. Low-voltage irregular pattern: REM/active sleep after NREM/quiet sleep: mixed diffuse theta (4–6 Hz, 40–60 μV) activity with few delta activity intermingled; (*1*) frontal sharp transients. Polygraphic parameters: EOG with rapid eyes movements; in EMG channel infrequent mylohyoid muscle brief contractions; in PNG irregular breathing

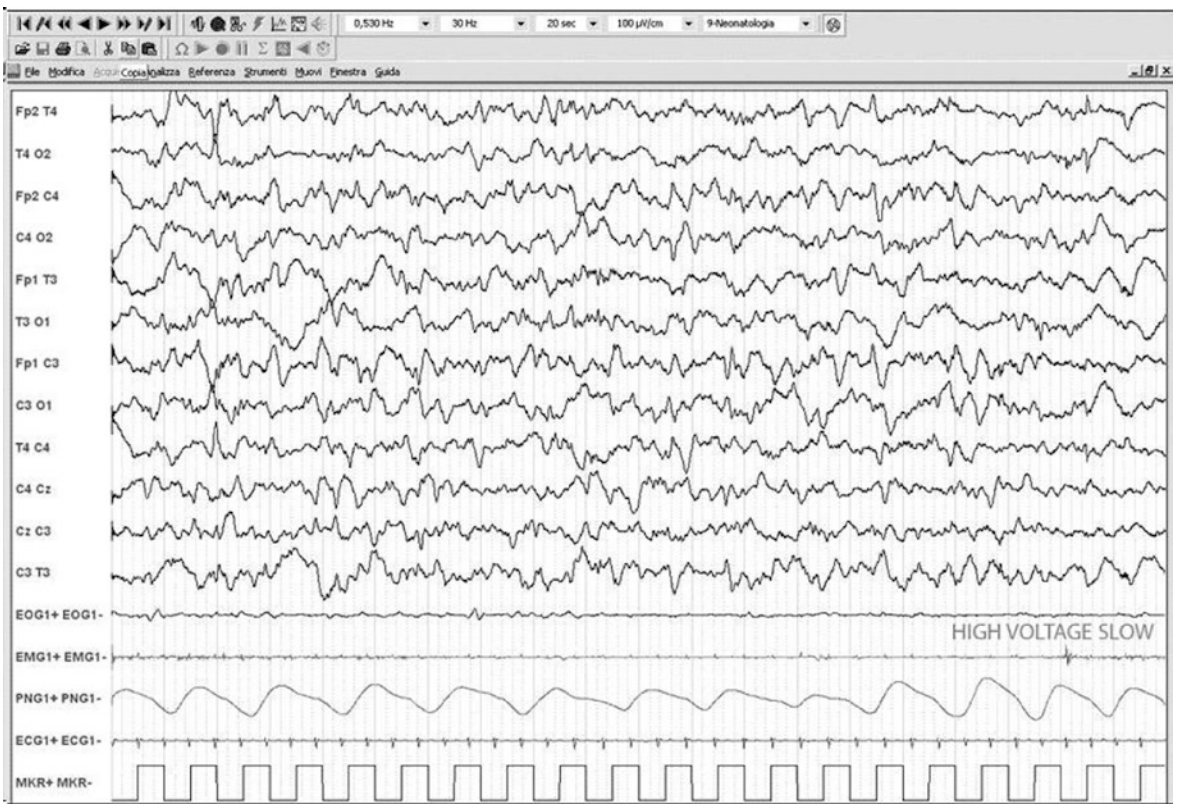

Fig. 11.30 40 weeks GA, 41 weeks CA. High-voltage slow (HVS) pattern: quiet sleep with diffuse and bilateral slow (delta-theta, 0.5–4 Hz, up to 200 μV) activity. Notice the most abundance of delta activity compared to Fig. 11.24. Polygraphic parameters in accordance with EEG pattern

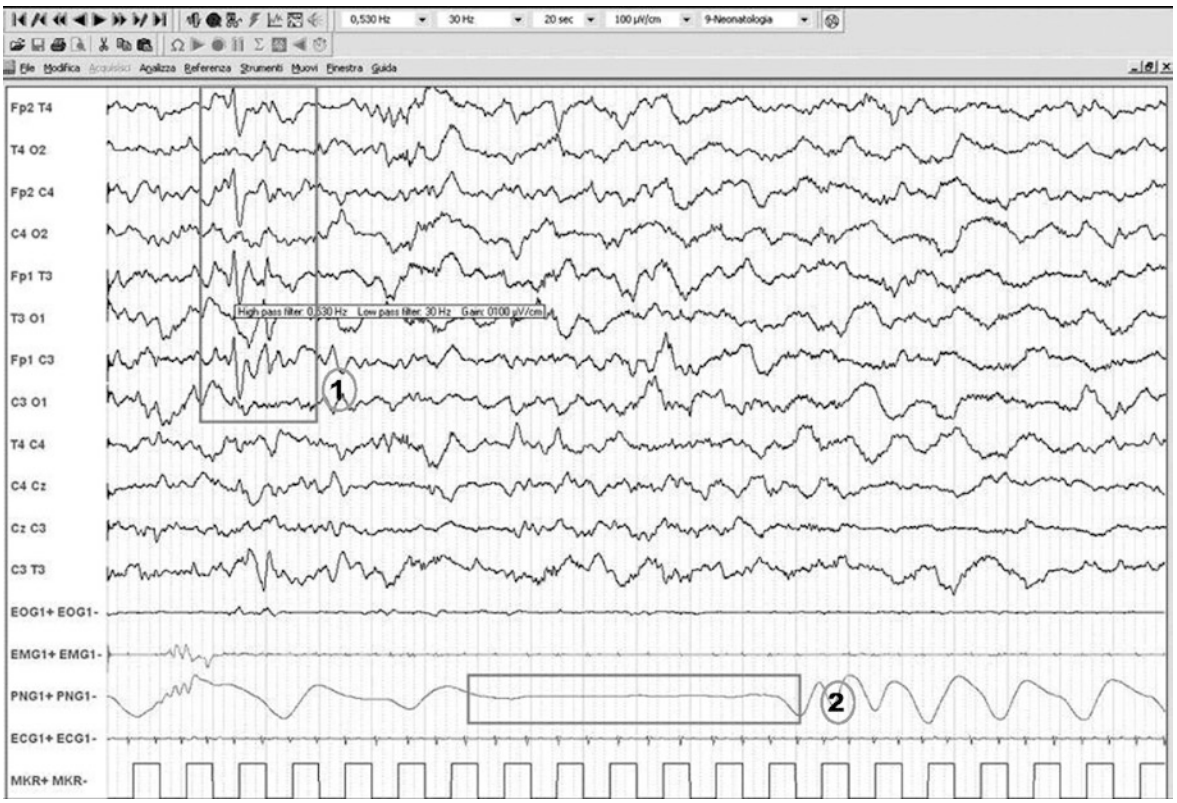

Fig. 11.31 40 weeks GA, 41 weeks CA. Transitional sleep from REM/active sleep to NREM/quiet sleep. (*1*) Bilateral frontal sharp transients; (*2*) 6 s breathing pause at the beginning of quiet sleep

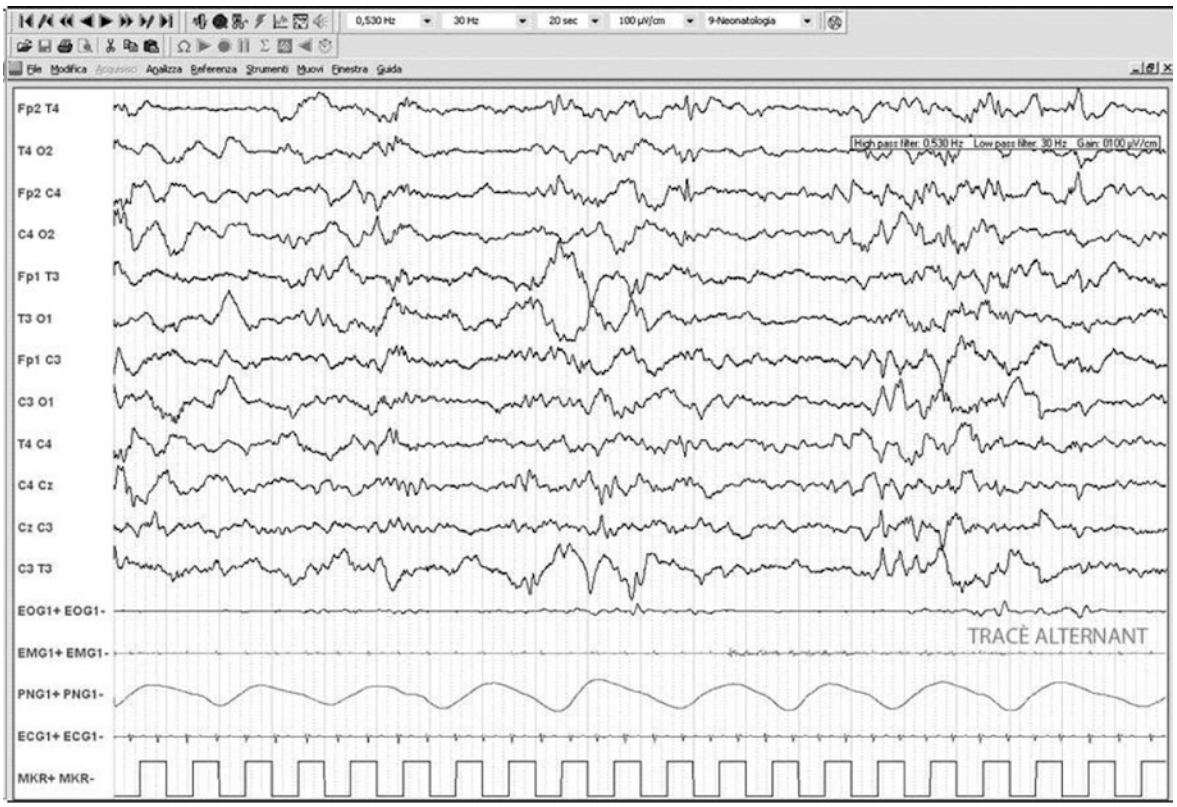

Fig. 11.32 40 weeks GA, 41 weeks CA. *Tracé alternant* pattern: within the bursts the most rapid and sharp activities disappeared compared to what is observed in previous CA (see Figs. 11.19 and 11.20). Burst amplitude is less than 200 μV. The interbursts activity has an amplitude up to 40–50 μV. Polygraphic parameters in accordance with EEG pattern

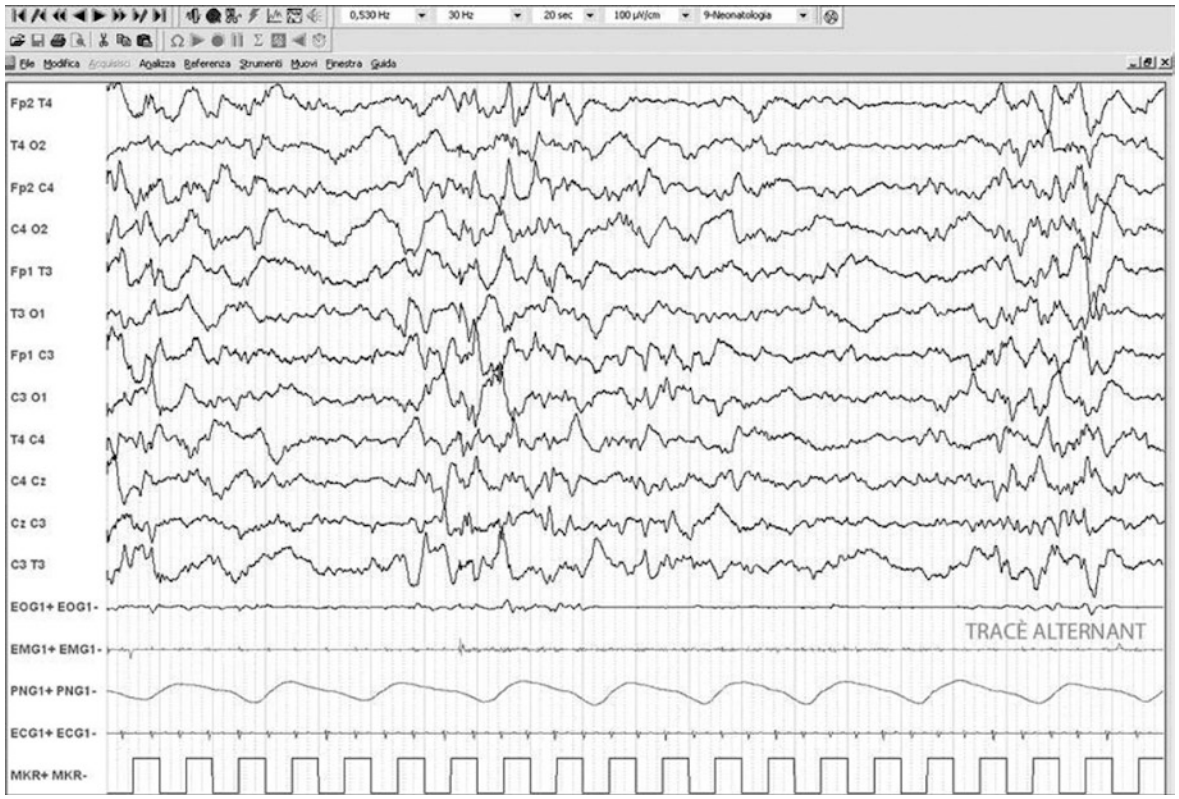

Fig. 11.33 40 weeks GA, 41 weeks CA. *Tracé alternant* pattern: the same characteristics of Fig. 11.32

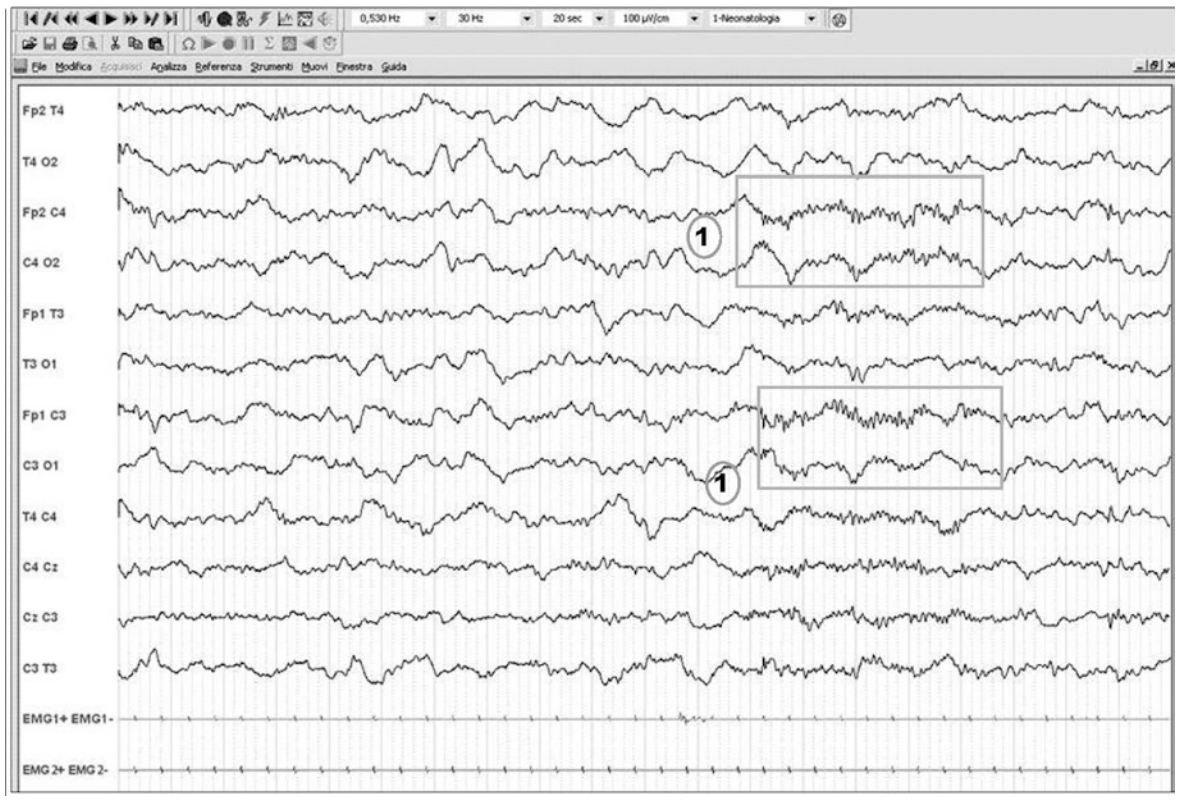

Fig. 11.34 39 weeks GA, 44 weeks CA. NREM/quiet sleep pattern with prevalence of diffuse and continuous theta-delta activity up to 200 μV; (*1*) rudimentary sleep spindles in the midline central region

Persistent interhemispheric synchrony. The background activity is reactive to stimulation.

Forty-four weeks: (by convention, it is considered the end of the neonatal period). In quiet sleep, the intermittent pattern progressively evolves toward a continuous slow pattern with the initial appearance of the sleep spindles (Fig. 11.34).

The table summarizes the main development grapho-elements in the EEG of the newborn, in parallel with the differentiation of behavioral states.

11.10 Amplitude-Integrated EEG (aEEG)

With the widespread use of the therapeutic hypothermia, there has been a significant impulse into the spreading of amplitude-integrated EEG (aEEG) use in neonatal intensive care units (NICU). It has some strengths such as the easiness of use [33], the immediate availability even for prolonged recordings, the compressed time scale, and the reduced montage, which shortens the technical time required for the execution and interpretation of recordings. aEEG is a reliable tool to monitor background brain activity in infants [34, 35], particularly if used with two channels and with the raw EEG data and if compared to the 1-h multichannel EEG recording [36, 37]. aEEG should be considered as a screening tool [38, 39] for seizure detection because there is general agreement regarding the fact that aEEG can miss infrequent, focal, low-amplitude, brief seizures with a duration <30 s [40–42]. For these reasons, reference to conventional or "raw" EEG should be made in order to increase its sensitivity and specificity whenever suspicious neonatal seizures are detected [43, 44]. Furthermore, the environment in NICU is not favorable for the neurophysiological monitoring of newborns because of the presence of several NICU equipment that can potentially lead to important artifacts. These can easily mimic a neonatal ictal discharge on aEEG, and sometimes raw EEG traces of the aEEG are not enough to clarify the real nature of these doubtful episodes [39, 45, 46].

Acknowledgments

- To the EEG technicians of the Pediatric Neurology Unit: Francesca Tabarelli, Deborah Meroni, and Gaetano Turi for their competence and sensitivity, constantly expressed in the management of newborns and in the acquisition of EEG recordings.
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- To Dr. Alfredo Radaelli and Davide Radaelli, for their essential advices in preparing the figures and the manuscript.

Appendix

Glossary

Activité moyenne: EEG pattern of the full-term newborn corresponding to wakefulness or to active sleep after quiet sleep state. Continuous electric activity with prevalent frequencies between 4 and 7 Hz (1–10 Hz), with an amplitude between 25 and 50 μV, with intermixed low-voltage delta activity.

- **Activity at 0–3 Hz**: slow waves at 0.3–3 Hz, of amplitude up to 300 μV, in the preterm newborn of less than 26 weeks GA.
- **Activity at 3–7 Hz activity**: occipital and isolated or in short runs of 1–2 s, of amplitude between 50 and 200 μV, in the preterm newborn of less than 27 weeks GA.
- **Activity at 8–13 Hz**: in short runs of 1–2 s, of amplitude between 25 and 30 μV, prevalent on Rolandic and occipital regions, in the preterm newborn of less than 28 weeks GA.

Anterior slow dysrhythmia (ASD): physiological pattern of the term newborn. In the neonatal period, the word dysrhythmia is still accepted—the ASD is characterized by a short sequence of 1–2 s of anterior slow waves at 2–3 Hz and of amplitude between 50 and 150 μV, synchronous (and asynchronous), sometimes associated with the frontal sharp transients.

Background activity: it includes the predominant frequencies and amplitudes with their variability, in relation to the spatial and temporal parameters, during the EEG recording. The background activity can be continuous or discontinuous depending on the presence, or not, in a given recording period, significant changes in the frequency, and/or amplitude of the electrical activity. However, the term "discontinuous" is used to define the recordings in which there are sections of significant voltage attenuation up to the absence of electrical activity. In relation to the clinical meanings of the "discontinuous tracing," the reader might refer to the iconography of this chapter and of the following chapter concerning the pathologic neonatal EEG recordings.

Conceptional age (CA): GA plus the weeks since birth; gestational age, measured from the time of the last menstrual period + chronological age.

Concordance and discordance: the presence or absence of regularly structured electrical and behavioral parameters, in relation to the specific state in the different GA.

Delta brush: physiological transient of the preterm and healthy newborn, with variable localization depending on the GA. It is a complex transient in which fast activity at 8–22 Hz, generally of low voltage (10–70 μV), immediately

precedes; it is superimposed or immediately follows a high-amplitude slow wave at 0.3–1.5 Hz, between 75 and 250 μV of amplitude. The characteristics of both fast activity and slow wave vary according to the degree of prematurity.

Dysmaturity: EEG characteristic due to the presence of an electric pattern corresponding to a lower GA than expected for that specific GA.

Encoches frontales (frontal sharp transients): typical physiological features since 35 weeks' GA, characterized by a biphasic wave (negative-positive) of amplitude variable between 50 and 200 μV, anteriorly localized, bilaterally synchronous and asynchronous; observable until the end of the neonatal period in quiet sleep state.

Gestational age (GA): the number of weeks since the beginning of the last menstrual.

High-voltage slow (HVS): slow pattern of high voltage—electric pattern of the full-term newborn during the quiet sleep state: frequencies between 0.5 and 4 Hz, of amplitude between 50 and 150 μV, irregularly rhythmic.

Liability: poorly definable or unstable behavioral state.

Low-voltage irregular (LVI): low-voltage irregular pattern—electric pattern of the full-term newborn, corresponding to the active sleep that appears after a quiet sleep phase: frequencies between 1 and 8 Hz with amplitude lower than 40–60 μV.

Mixed activity: electric pattern of the full-term infant corresponding to the active sleep that generally appears at the beginning of a sleep cycle. It is constituted by the moyenne activité pattern over which theta-delta activity at 2–4 Hz is superimposed, with an amplitude of less than 100 μV.

Neonatal period: the first 4 weeks of life for the full-term newborn (40 weeks' GA) and in any case up to the 44 weeks of GA for the preterm newborn:

- **Preterm newborn**: born before 37 weeks of GA.
- **Term newborn**: born between 38 and 42 weeks of GA.
- **Post-term newborn**: born over 42 weeks of GA.

Paroxysmal: mode of appearance of an electrical event that begins and ends abruptly, clearly distinguishing itself from the background activity, generally of higher but sometimes of lower amplitude.

Positive and negative (temporal/Rolandic sharp waves): phase reversal in a bipolar derivation with variable localization, generally isolated and with voltage lower than 100 μV. Otherwise, they have a connotation of focal pathological transients and/or white matter involvement (positive Rolandic sharp waves).

Reactivity: modification of the background activity after external stimulation.

Sharp transients: spike or sharp wave transients that maintain the same morphological definition usually used in electroencephalography at any age but in the neonatal period are frequently typical physiological features of specific GA.

State: well-defined behavioral modality characterized by physiological events that occur in specific epochs of postnatal life both in the full-term and in the preterm newborn, with a predictable and cyclical trend.

Temporal spike and sharp waves: physiological elements, of variable amplitude, peculiar to an age between 29 and 32 weeks' and at 37 weeks' GA (multifocal interburst sharp waves).

Temporal theta burst or temporal sawtooth: peculiar physiological elements of the preterm newborn <33 weeks' GA—short sequences of 3–5 s of diffuse rhythmic activity at 4–7 Hz, of amplitude between 50 and 250 μV, synchronous on the same hemisphere or more evident in the temporal region, bilaterally synchronous and asynchronous.

Tracé alternant (TA, alternating tracing): electric pattern of the full-term newborn observable in the quiet sleep—epochs of 3–8 s with delta activity at 0.5–3 Hz of amplitude between 50 and 200 μV, with superimposed fast activity of lower voltage, interspersed with sections of 3–8 s with theta activity at 4–6 Hz of amplitude between 25 and 40 μV.

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