Abnormal Neonatal Patterns

22

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22.1 Abnormal Neonatal EEG

The distinctive features of the neonatal electroencephalogram (EEG), the development of the behavioral states and of the EEG patterns from 27 weeks of conceptional age (CA) to the end of the neonatal period have been described in the first part of this Manual. Particular attention has been devoted to the development of the EEG features as a function of the different stages of the central nervous system development.

This chapter is dedicated to the description of the most characteristic artifacts and the abnormal EEG findings in the neonatal age. As in the previous chapter, we have emphasized the iconographic material, taken from EEG recordings carried out within the daily clinical practice of the authors at Buzzi Hospital in Milan (Pediatric Neurology Unit and Neonatal Intensive Care Unit) and at University Hospital of Parma (Pediatric Neurophysiology Lab and Neonatal Intensive Care Unit). The caption of the figures will report the anamnestic, clinical, and instrumental data related to the clinical cases described, in order to underline and confirm the importance of a complete integration among clinical, neurophysiological, and neuroimaging data in the approach of newborns with neurological impairments.

22.2 Introduction

In the previous chapter, it has already been emphasized that the EEG, together with the clinical and neuroimaging data, has both a diagnostic and an early prognostic meaning in the neonatal age [1, 2]. It is clear how the EEG allows an essential evaluation of the degree of development and functionality of the central nervous system (CNS), becoming one of the actions of a multispecialistic management of a newborn with neurological and possibly systemic diseases.

The current neonatal neurology assumes the need to integrate the information acquired by EEG recordings with both the clinical and neuroradiological findings at the same time, especially for the "abnormal EEG pattern," before giving a prognosis. This integrated approach through the three points of observations (clinical, neurophysiological, and anatomo-morphological) allows to provide the clinician and the neonatologist, in this context, with important information to correctly manage the pathology in progress.

22.3 Extra Cerebral Artifacts

In Figs. 22.1–22.18, a series of images related to newborns with and without neurological pathology are shown. In the caption of each single image, the symbol "A" indicates tracings with artifacts, the gestational age ("GA") expressed in weeks, and the age at the time the study was carried out (CA); finally, the type of artifact and the location is described.

For the visual analysis and interpretation of the EEG recording, it is essential to distinguish the electrical activity coming from the brain and from the extracerebral artifacts [3]. Although frequently extracerebral artifacts are easily identifiable, there are some artifacts that may not be recognized as such, thus leading to false-positive recognition of pathological findings, which can result in erroneous interpretation of the recording and consequently lead to an incorrect clinical management of the newborn.

There are artifacts secondary to the technical-instrumental characteristics of the recording ("technical artifacts") and artifacts secondary to physiologic manifestations of the child ("biological or physiological artifacts"). As for the "technical artifacts" related to the recording conditions, in addition to the faulty contact of the electrode (Figs. 22.1 and 22.2), to field problems related to the electrode wire itself or to the EEG connection cable (Fig. 22.10), and to the presence of alternating current (Fig. 22.1), it is known that in Neonatal

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Intensive Care Units, there are often several monitors and other devices, including infusion pumps and mechanical ventilators (Figs. 22.3 and 22.4), which can interfere with the acquisition of the EEG signal. The "biological or physiological artifacts" are instead related to the patient. Several examples of artifacts spreading to the scalp are illustrated: the electrical signal generated from the electrocardiogram (EKG, Fig. 22.9); more or less massive or rhythmical muscle contractions (Fig. 22.12); diffuse or segmental tremors at low, medium, or high frequency (Figs. 22.13–22.16); the anterior fontanel pulsations (Fig. 22.5) or of the caregiver who carries it; eye movements (Fig. 22.8); suction and hiccup (Figs. 22.11, 22.12, 22.17, and 22.18); sweating (Figs. 22.5 and 22.13); movements caused by parents rocking the newborn (Figs. 22.6 and 22.7).

The presence of the EEG technician, appropriately trained for the newborn management, appears essential in the definition and elimination of technical artifacts. On several occasions, however, physiological artifacts cannot be eliminated, but they must nevertheless be identified and described in the report that accompanies the recording. Furthermore, polygraphy helps to distinguish artifact from an activity of cerebral origin: the eye movements (Fig. 22.8) and the rhythmic deflection of the QRS cardiac complex are detected on the EEG traces with the same deflection (Fig. 22.9), the eye artifact is generally irregular and of high amplitude, the EKG artifact is rhythmic and of high frequency, and the breathing movements detected by the pneumogram and the rhythmic activity produced by the ventilator machines generally induce a slow rhythmic deflection (Figs. 22.3 and 22.4). On the other hand, rocking the newborn causes a slow and intermittent, but irregular, sinusoidal activity on the EEG traces (Figs. 22.6 and 22.7). Sucking, especially when the baby's head is rotated with the temporal electrode close to the bed, can result in a double artifact, with rapid activity due to muscle contraction and slow rhythmic activity linked to the movement of the mandibular segment (Figs. 22.1 and 22.12).

The simultaneous video recording is an important technological acquisition, above all for the possibility to review offline what happened during the recording [4], but this cannot absolutely exclude the visual monitoring of the recording in progress. Therefore, once the child is prepared for the recording, the EEG technician must check the characteristics of the recording and is responsible for the recording that he provides to the physician for the final interpretation.

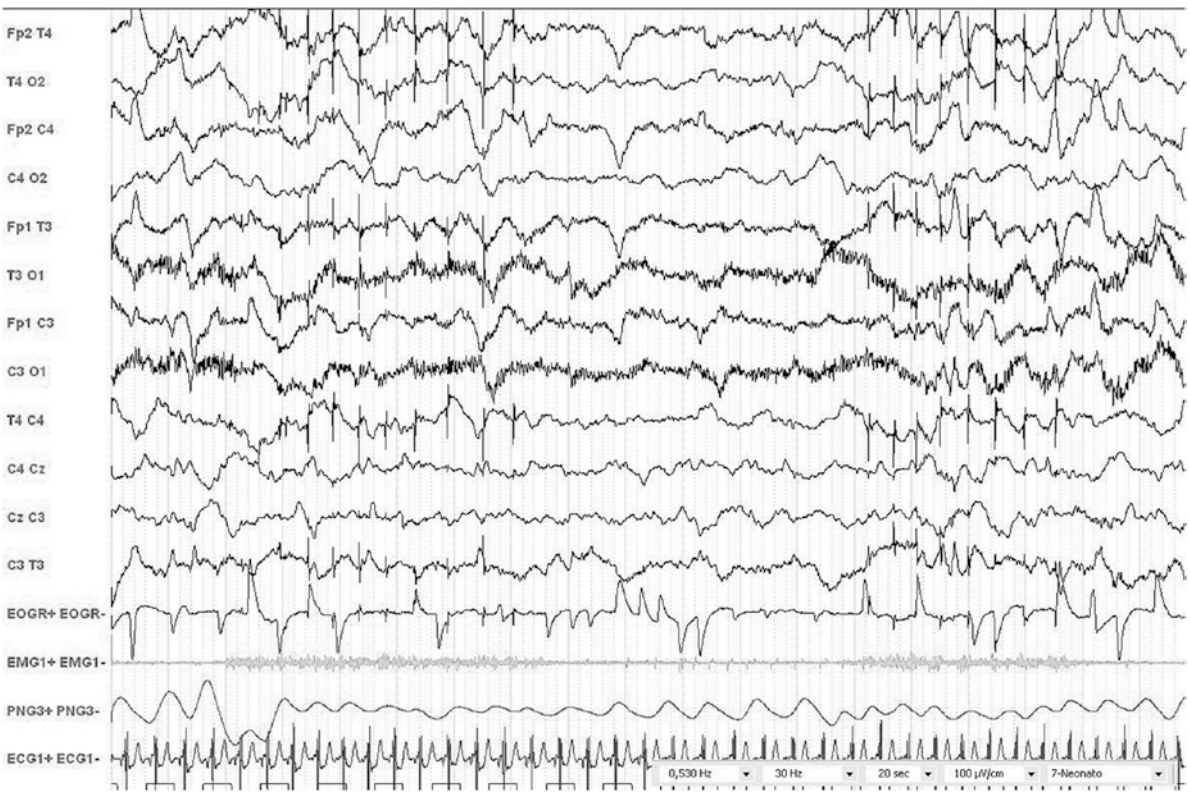

Fig. 22.1 40 weeks GA, 40.2 weeks CA. Healthy newborn. Wakefulness, open eyes. Sucking artifact in T4 and T3: rhythmic fast spikes strictly related to the rhythmic contraction of mylohyoid muscle in EMG channel. Low-voltage fast activity muscle artifact in O1 and less evident in Fp1–Fp2. Alternating current artifact (50 Hz) of variable amplitude involving left side electrodes (mostly O1) and Fp2, produced by high skin-electrode interface impedance

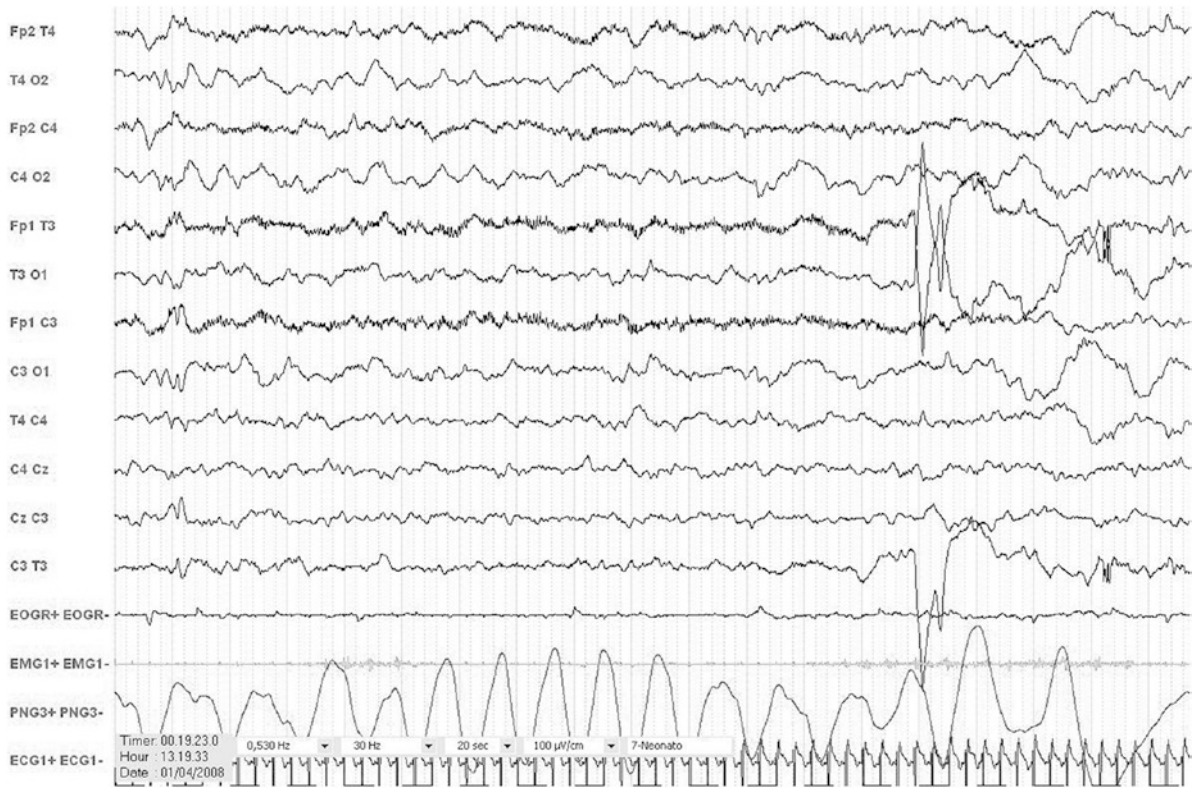

Fig. 22.2 39 weeks GA, 39.4 weeks CA. Healthy newborn. Wakefulness, open eyes. Artifact in T3 with fast spike >high amplitude and sharp slow wave produced by unstable T3 electrode: abnormal cable-electrode connection. Artifact in Fp1–Fp2 with fast continuous and low-voltage activity produced by frontal muscle contraction

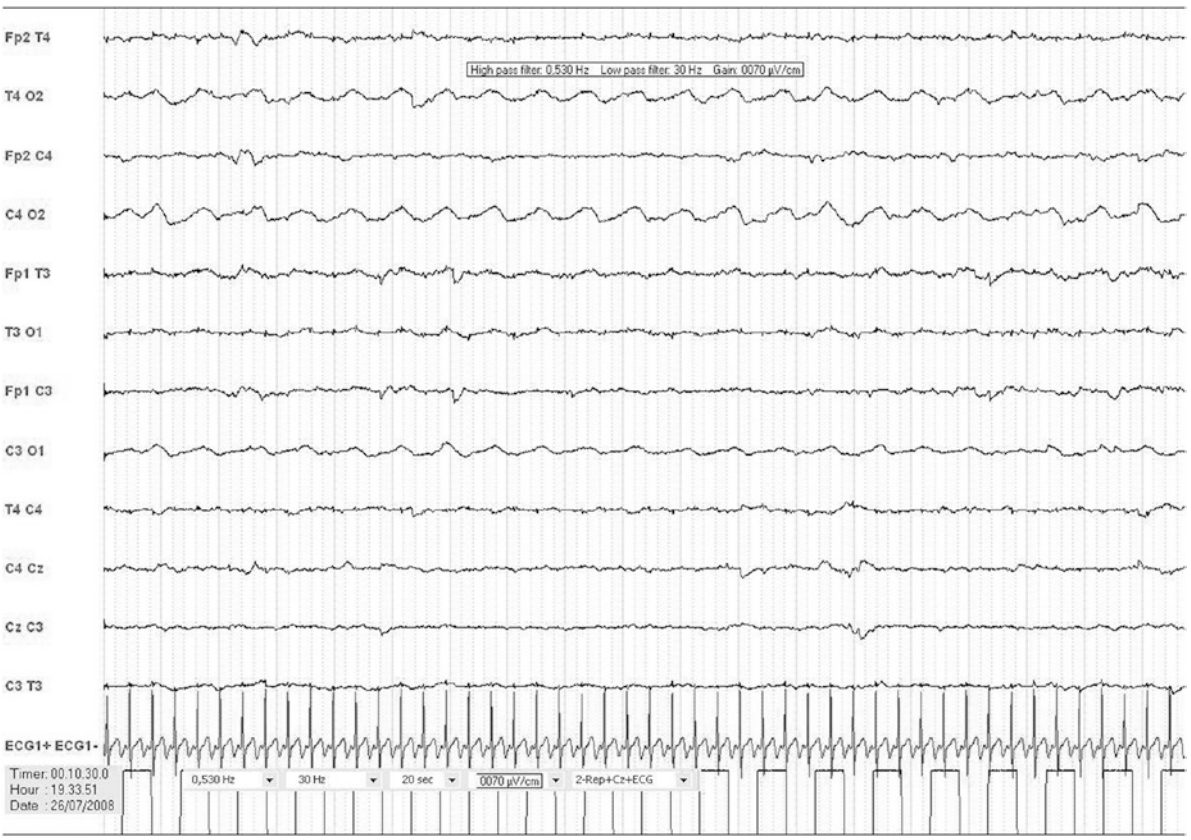

Fig. 22.3 32 weeks GA, 33.1 weeks CA. Coma in newborn affected by intraventricular grade IV hemorrhage. Constantly inactive tracing. Artifact in O2 and less evident in O1: slow and rhythmic activity, synchronous with head movements and with mechanical ventilation. Low-voltage EKG artifact in several leads

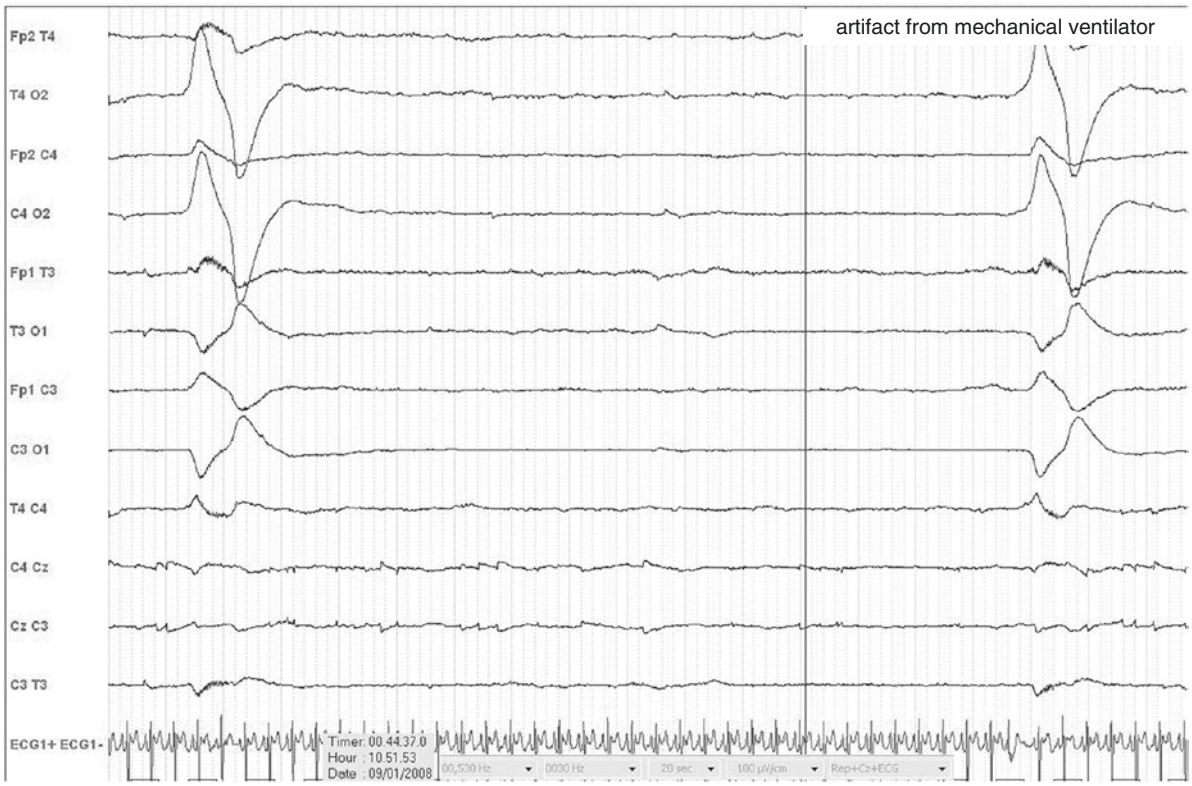

Fig. 22.4 27 weeks GA, 42.3 weeks CA. Coma in newborn after prolonged cardiac arrest. Mechanical ventilation. Constantly inactive tracing. Complex artifacts: short sequence of low-voltage fast activity (frequency over 25 Hz) superimposed on a diphasic and high-amplitude slow deflection. The same artifact repeats after 14 s related to the trigger of the mechanical ventilation system

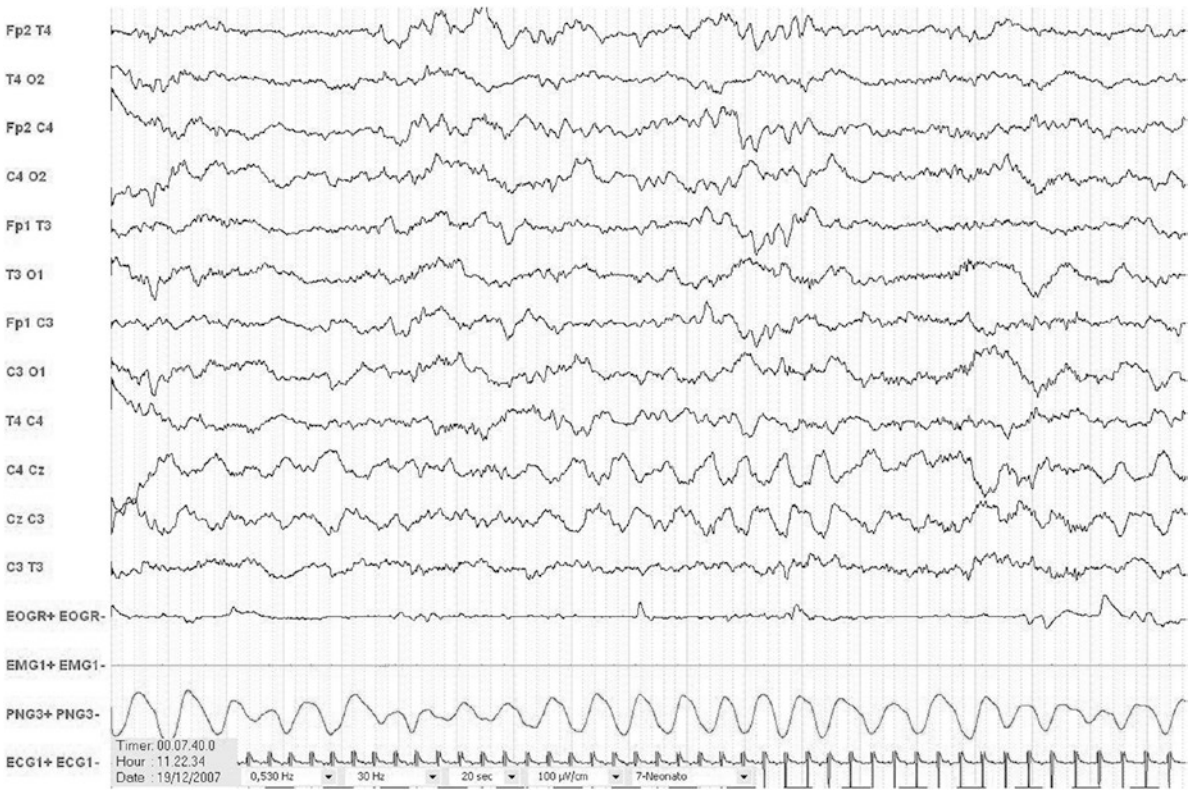

Fig. 22.5 36 weeks GA, 38.3 weeks CA. Healthy newborn. Cz artifact with rhythmic deflections having the same frequency of abdominal respiration and reflecting increasing/decreasing impedance in an unstable electrode, partially placed near the anterior fontanel. Tracé alternant (quiet sleep) is the EEG pattern in this newborn, while polygraphic parameters (presence of eye movements and irregular respiration) are consistent with active sleep. Moreover a very slow deflection artifact is present in all leads, due to excessive sweating

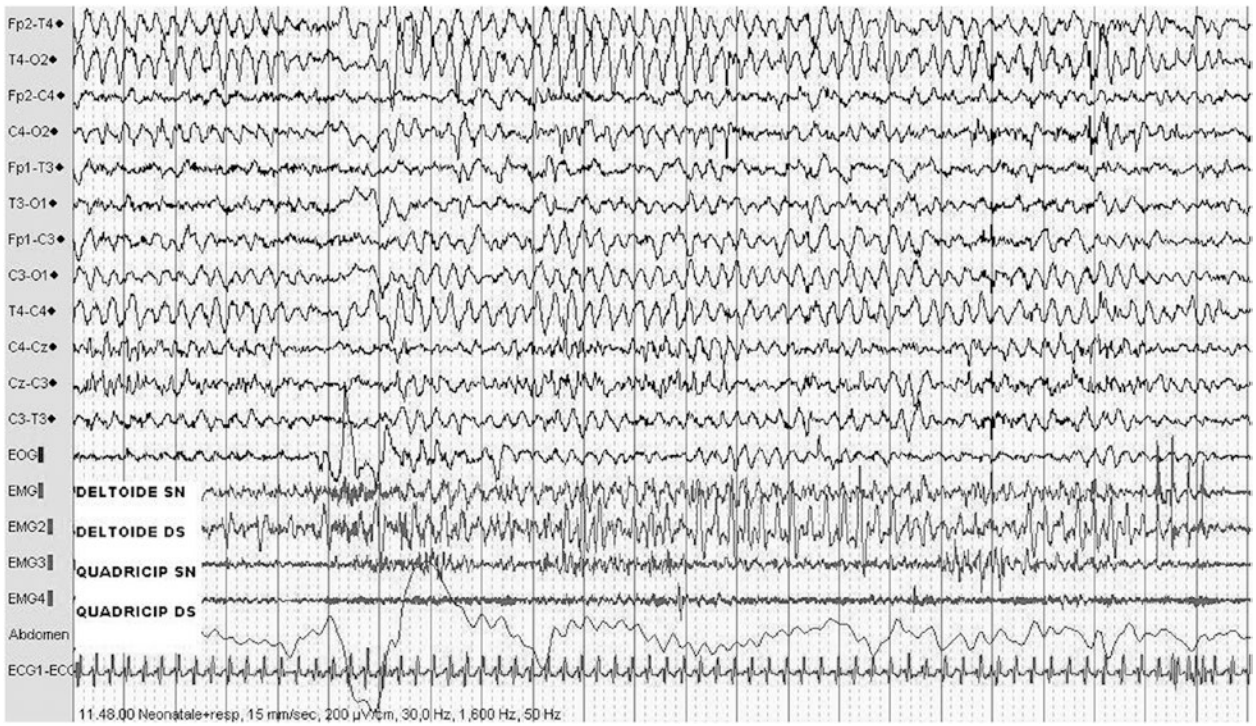

Fig. 22.6 40 weeks GA, 40.3 weeks CA. Healthy newborn. The infant is difficult to console. Artifacts in all leads more prominent in T4, C4, and C3 with high-voltage rhythmic activity, mimicking the same fluctuation frequency of polygraphic electrodes (EMG and abdominal transducer) produced by parent's rocking of the child

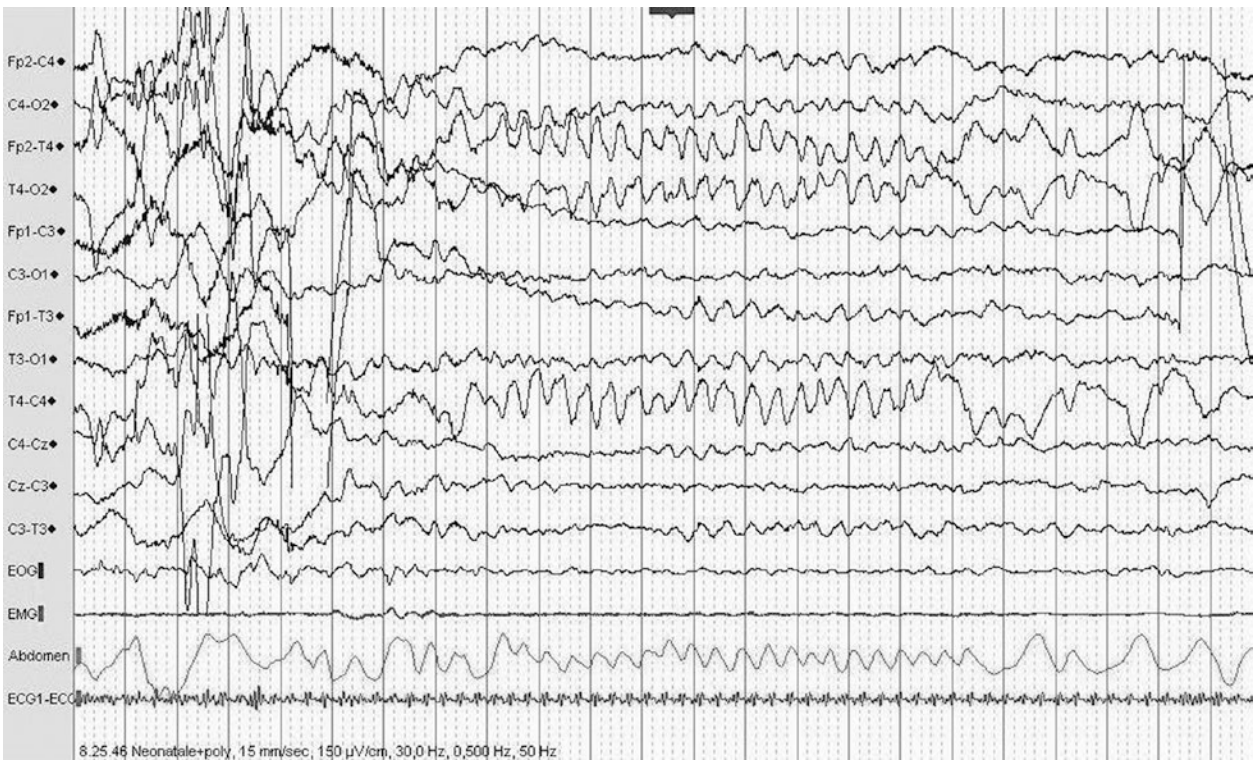

Fig. 22.7 38 weeks GA, 39 weeks CA. Awake, difficult to console. Same rocking artifact only in T4 which results in electrode instability. In the right side of the figure, T4 electrode "pop" is recognized by irregular high-voltage slow waves

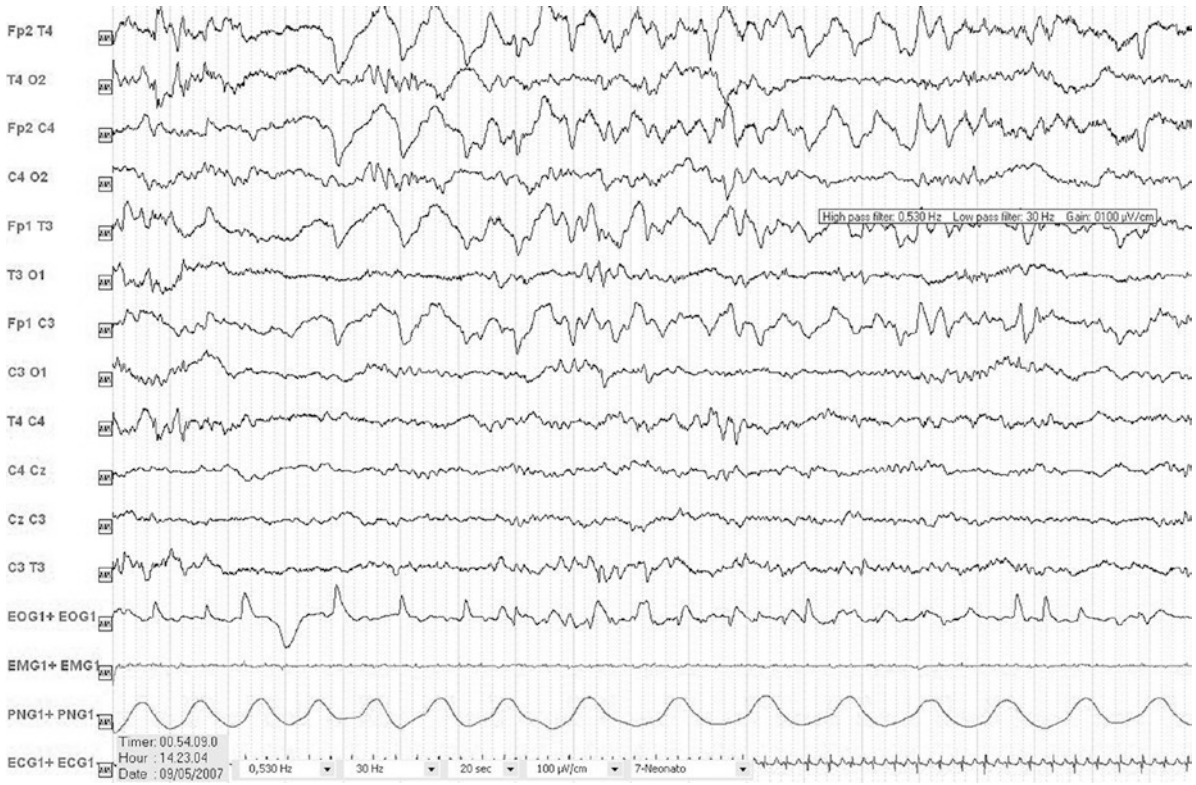

Fig. 22.8 39 weeks GA, 39.2 weeks CA. Healthy newborn. Quiet alert, open eyes. Ocular movement artifacts limited to Fp1 and Fp2 (placed too low in the forehead): slow and sharp polymorphic deflections, synchronous with eye movements detected by electrooculogram

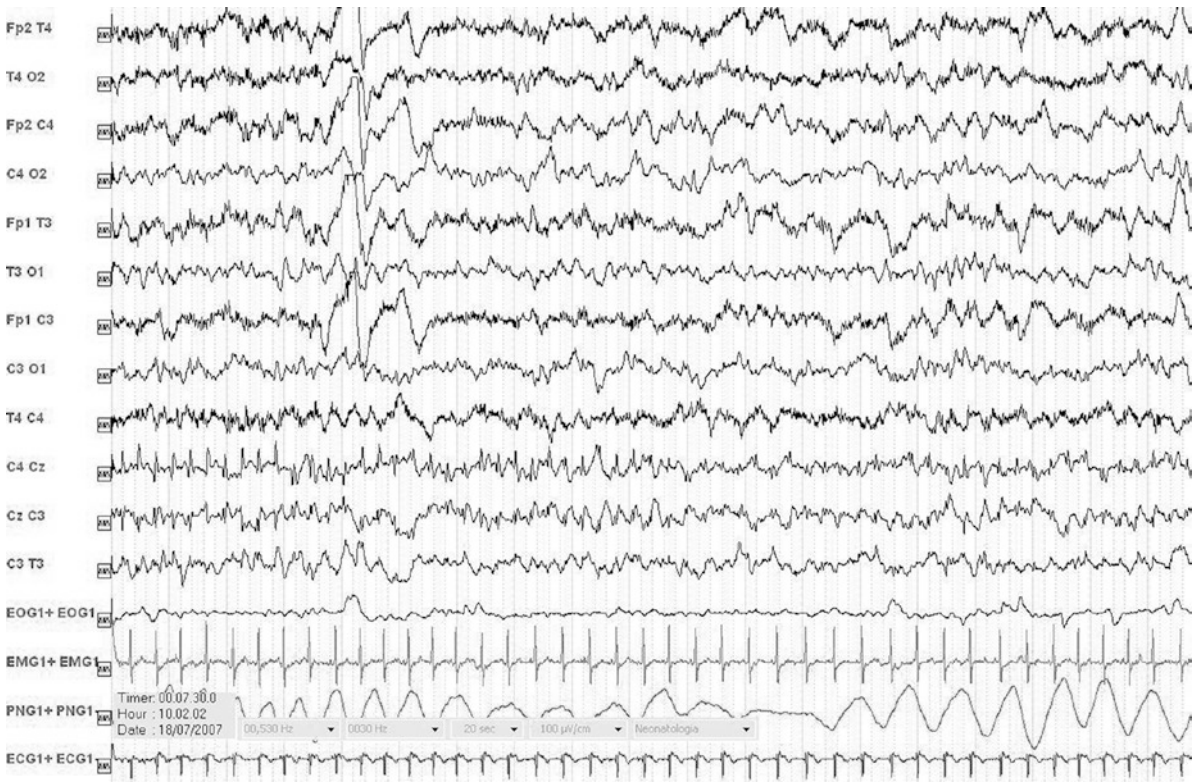

Fig. 22.9 36 weeks GA, 38.5 weeks CA. Healthy newborn. Quiet alert, eyes open and closed. Cz artifact in which EKG complex is recognized even in mylohyoid muscle. In Fp1, Fp2, and T4 fast low-voltage activity produced by muscles. High-voltage vertical deflection produced by eye movements in Fp1 and Fp2

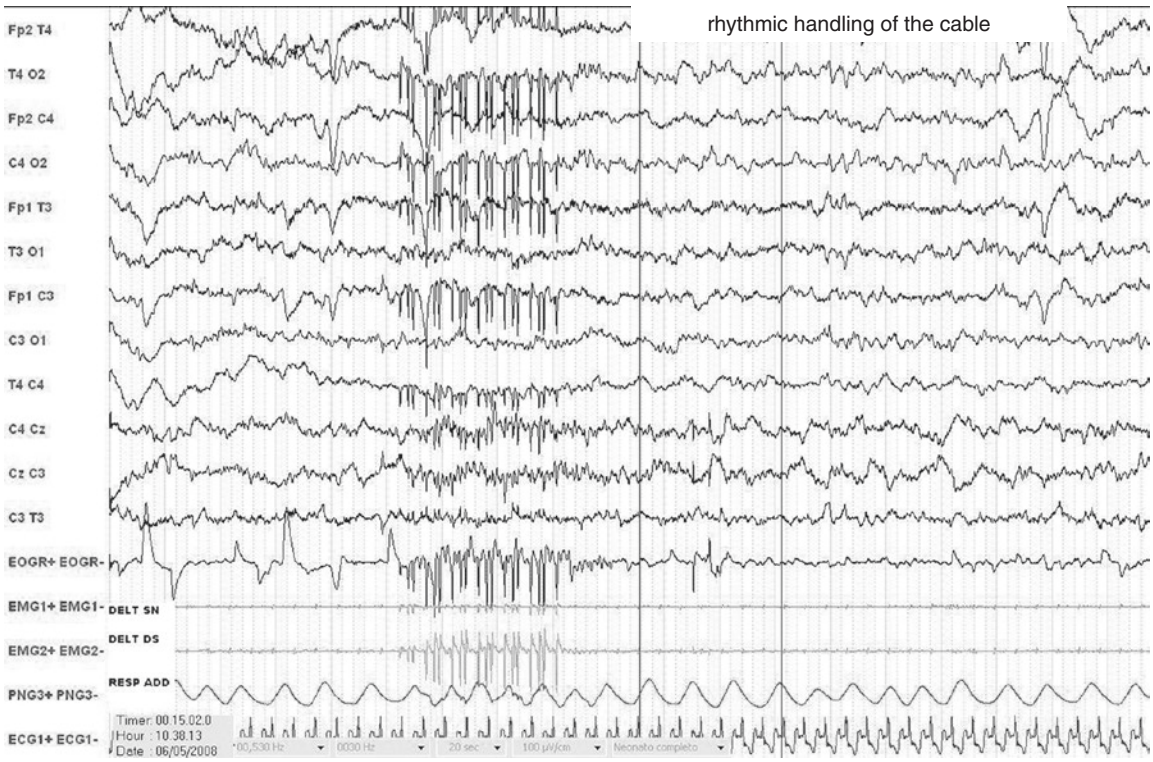

Fig. 22.10 38 weeks GA, 40 weeks CA. Healthy newborn. Quiet alert, open eyes. Electromagnetic field artifacts in all recording leads induced by rhythmic handling of the cable connecting to the head-box. NB: Potentials recognized in EMG channels (right and left deltoid muscles) are not the expression of child movements

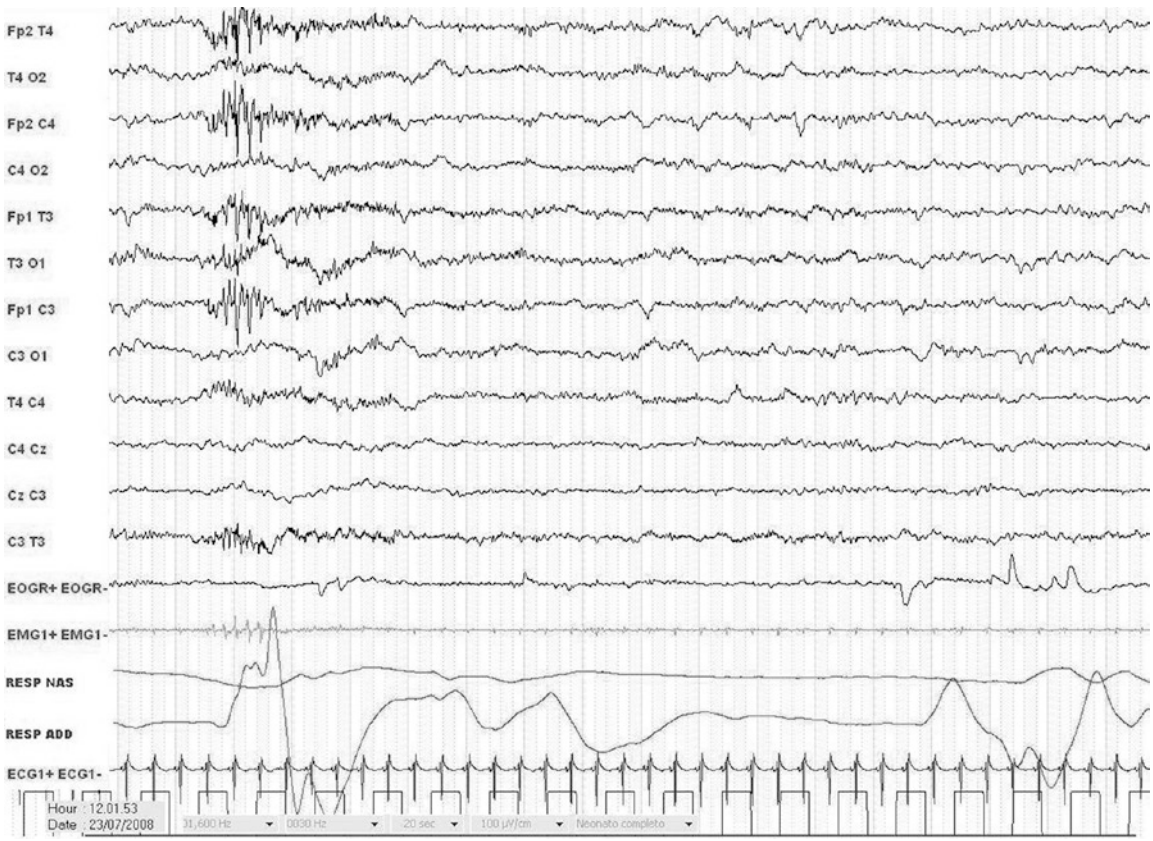

Fig. 22.11 36 weeks GA, 38 weeks CA. Healthy newborn. Active sleep after quiet sleep. Complex artifacts induced by hiccup, represented by a high-voltage deflection in the abdominal respiration channel. Five rhythmic chest contractions are recorded simultaneously in EMG1 (mylohyoid muscle); they produce an interfering fast low-voltage muscular activity intermingled with single rhythmic spike waves induced by chest movements

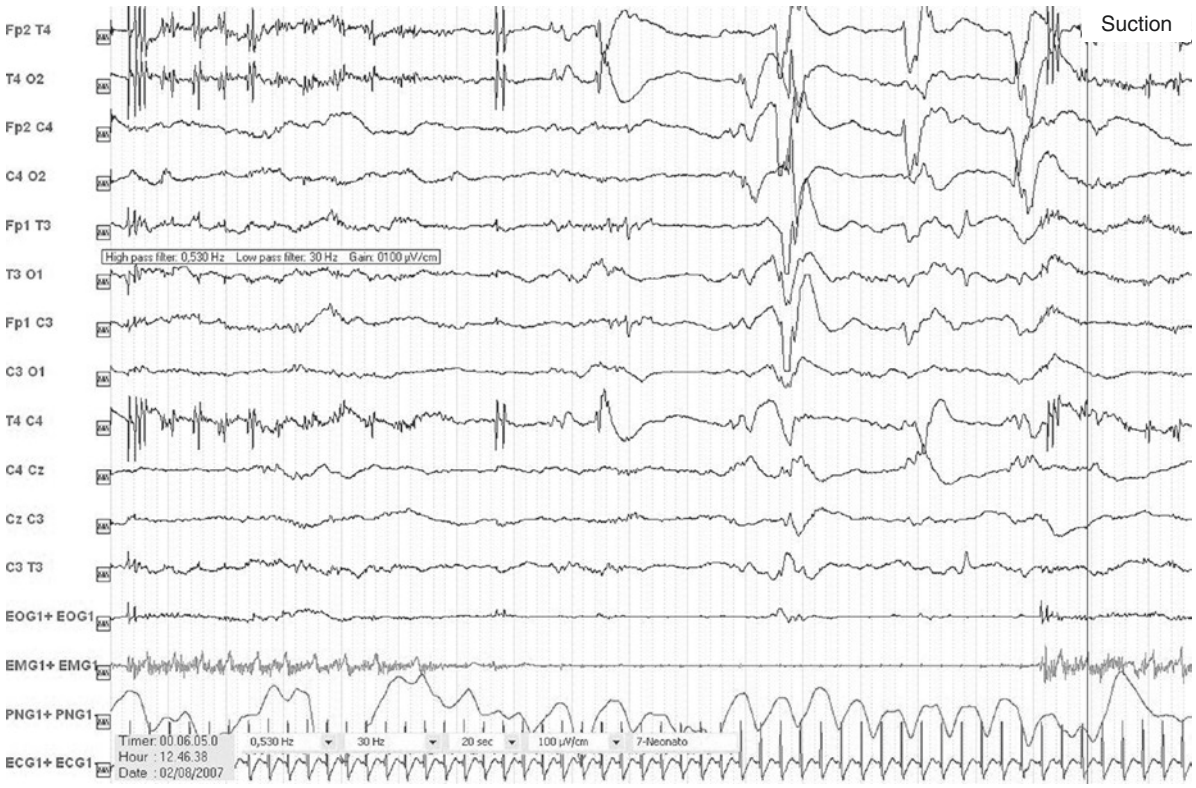

Fig. 22.12 31 weeks GA, 31.5 weeks CA. Intraparenchymal frontotemporal hemorrhage in the right hemisphere. In wakefulness T4 artifact (less evident in T3) produced by sucking (see mylohyoid muscle in EMG1) with rhythmic muscular spike superimposed to an interfering activity of 6-s duration, occurring again with the same morphology after 11 s. In T4 it is also present a slow and high-voltage spike-wave complex of cerebral origin evidence of intraparenchymal injury

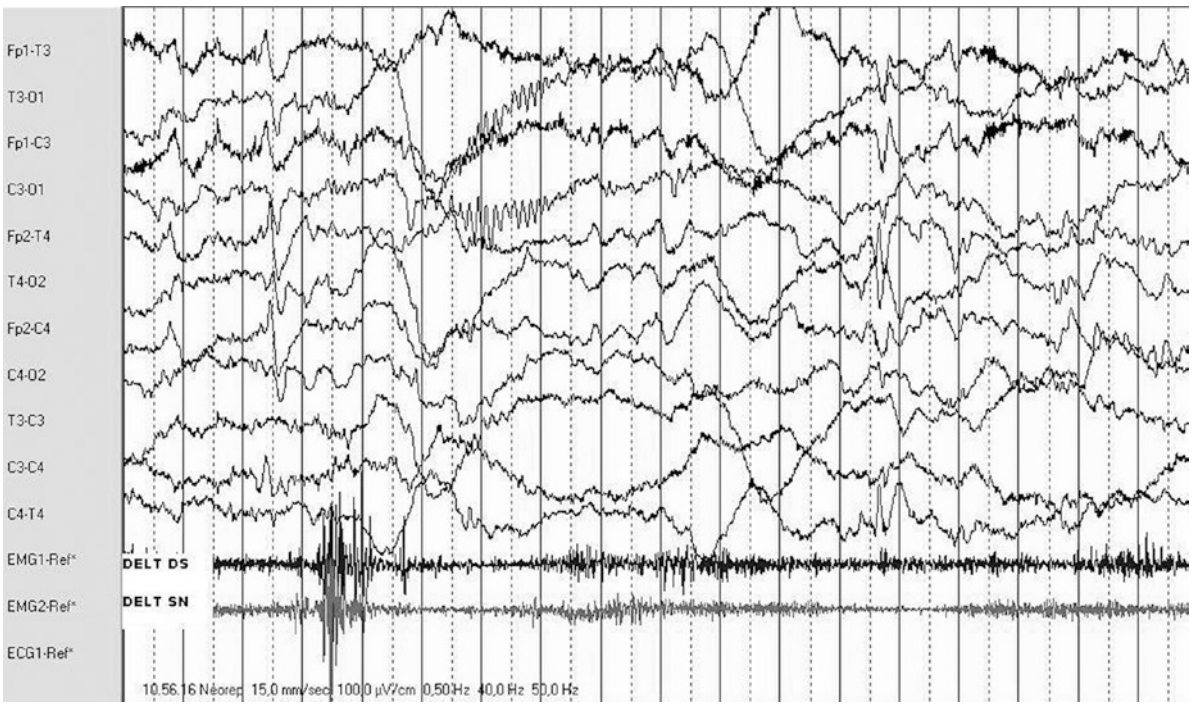

Fig. 22.13 40.4 weeks GA, 41 weeks CA. Healthy newborn with jitteriness, awake. O2 artifact in which a rhythmic 7 Hz oscillation, induced by shaking limbs tremor, produces rhythmic oscillation of the head. It is overlapping with an interfering fast low-voltage activity originating in muscles, more evident on the left side, induced by jitteriness that produces in the right and left side increased and sustained hypertonus of deltoid muscles. Moreover a very slow deflection artifact is present in all leads, due to excessive sweating

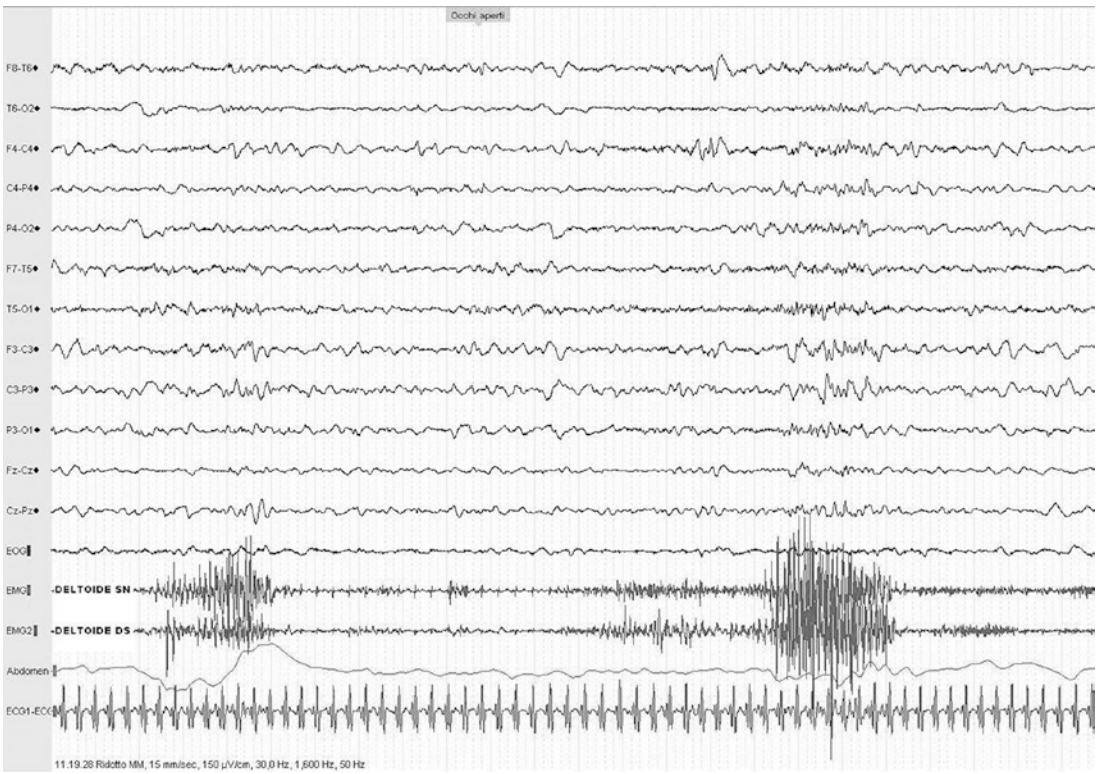

Fig. 22.14 40 weeks GA, 40.3 weeks CA. Healthy newborn, tremulousness. Quiet alert. Two high-frequency short runs of tremors in deltoid muscles. Increased low-voltage fast activity over temporal and frontal regions. On the left side electrodes, a 9 Hz fast and rhythmic activity synchronous with head movement induced by tremor

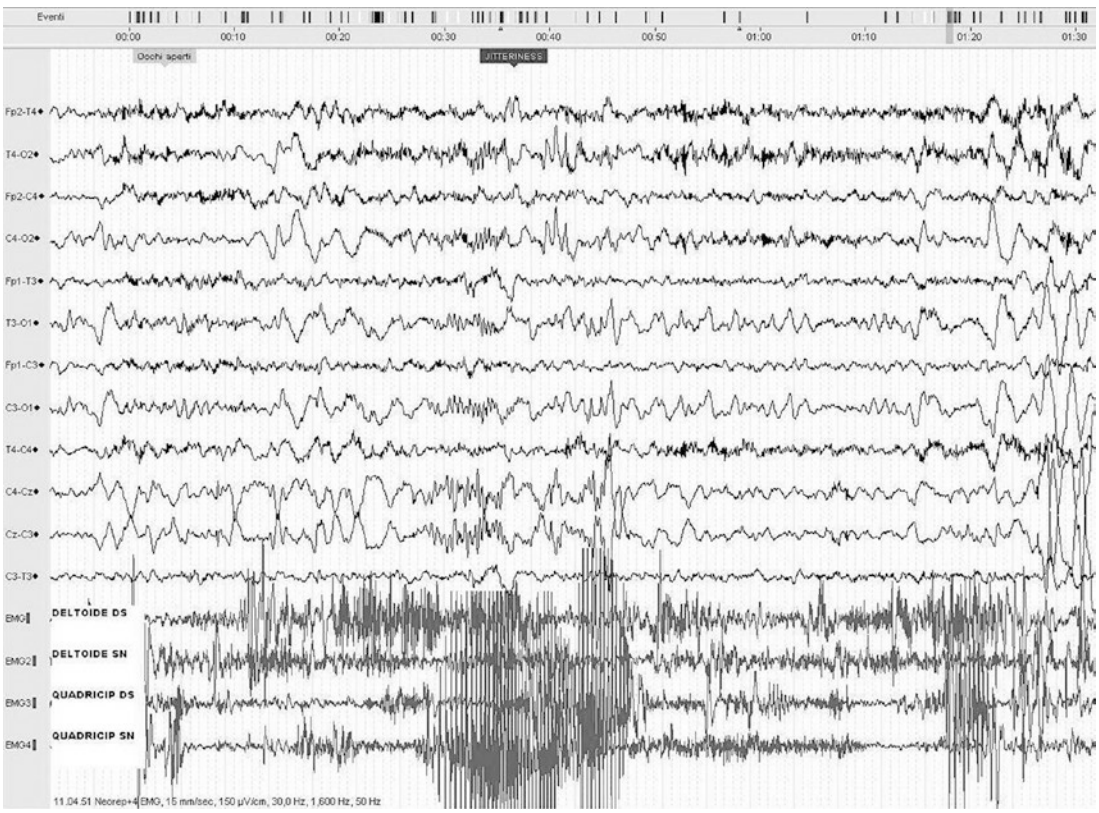

Fig. 22.15 33.2 weeks GA, 37 weeks CA. Healthy newborn. Awake, open eyes. Jitteriness. In Cz, O1, and O2, the protracted and rhythmic high-frequency movements of the four limbs, spreading to the scalp, induce a 10–18 Hz rhythmic activity synchronous with the movements. This activity intermingled with the interfering and generalized low-voltage activity originating from the muscles, produced by the generalized hypertonus shown on muscular polygraphy, unrelated to jitteriness

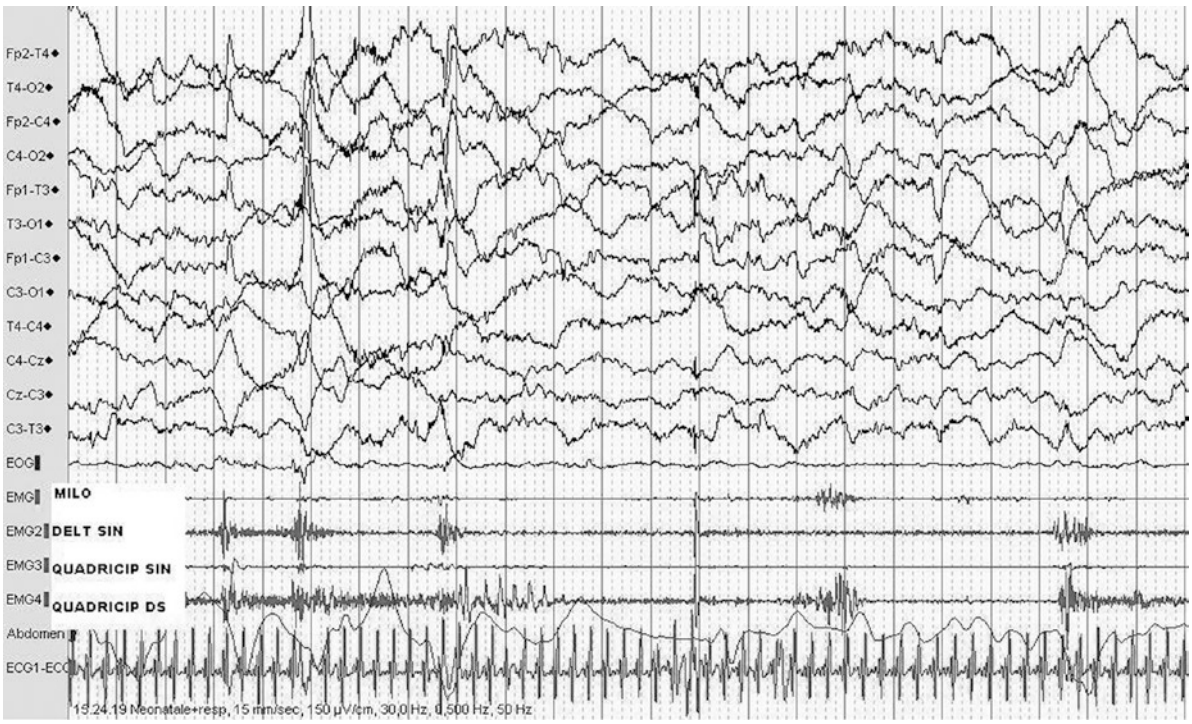

Fig. 22.16 39 weeks GA, 39.6 weeks CA. Healthy newborn. Active alert. Several paroxysmal non-epileptic jerks are distinguished in the polygraphic leads: myoclonia, spasm, and spasm with protracted tonic contraction. Polymorphic artifacts are associated over the scalp, in which is constantly present a vertical signal deflection expression of the paroxysmal movement onset and followed by return to baseline, depending on the features of the different movements

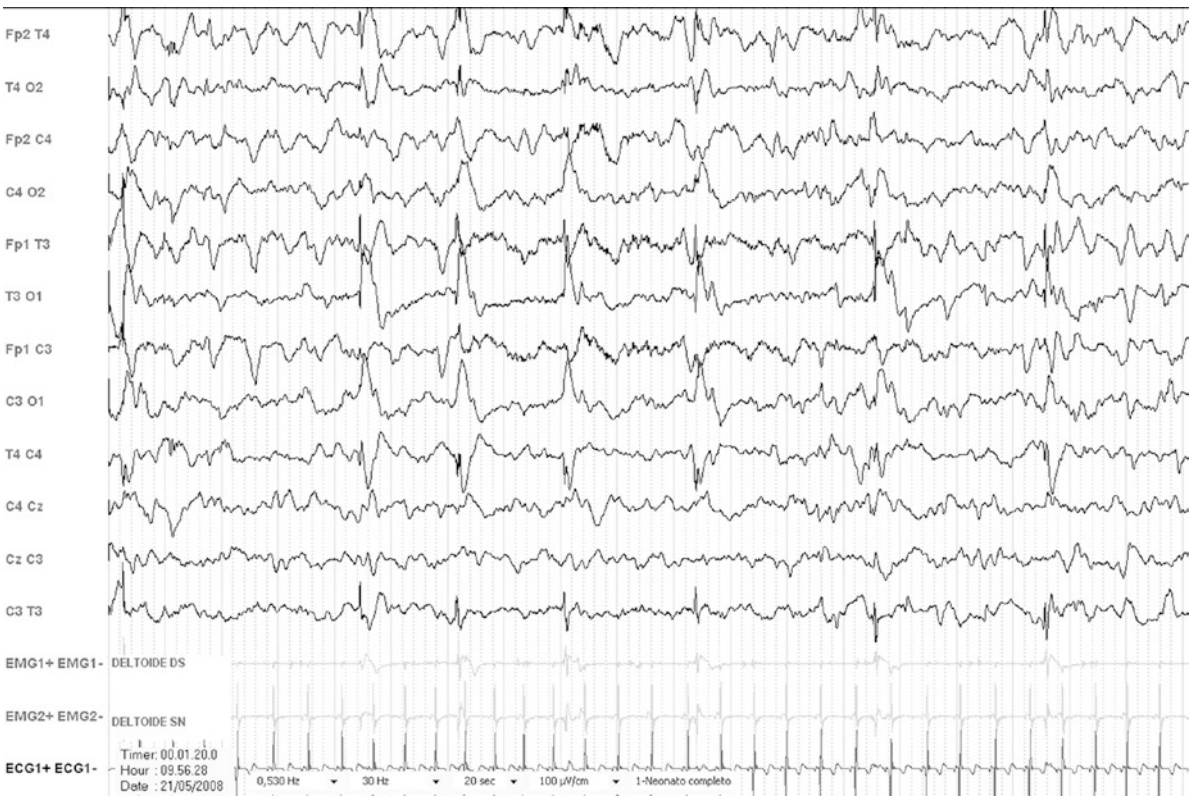

Fig. 22.17 40 weeks GA, 41 weeks CA. Brother of a patient with undiagnosed congenital encephalopathy. At birth arthrogryposis of the limbs and drowsiness. Beginning on the 1st day of life massive contraction of superior limbs and hiccup. In the figure drowsiness and theta-delta mixed background activity, without significant asymmetry. Polygraphic recordings of deltoid muscles permit to detect bilateral high frequency contractions. Seven events are recorded in 18 s coinciding with an anterior and temporal bilateral artifact over the scalp. This artifact is characterized by a vertical fast deflection followed by an angular slow wave

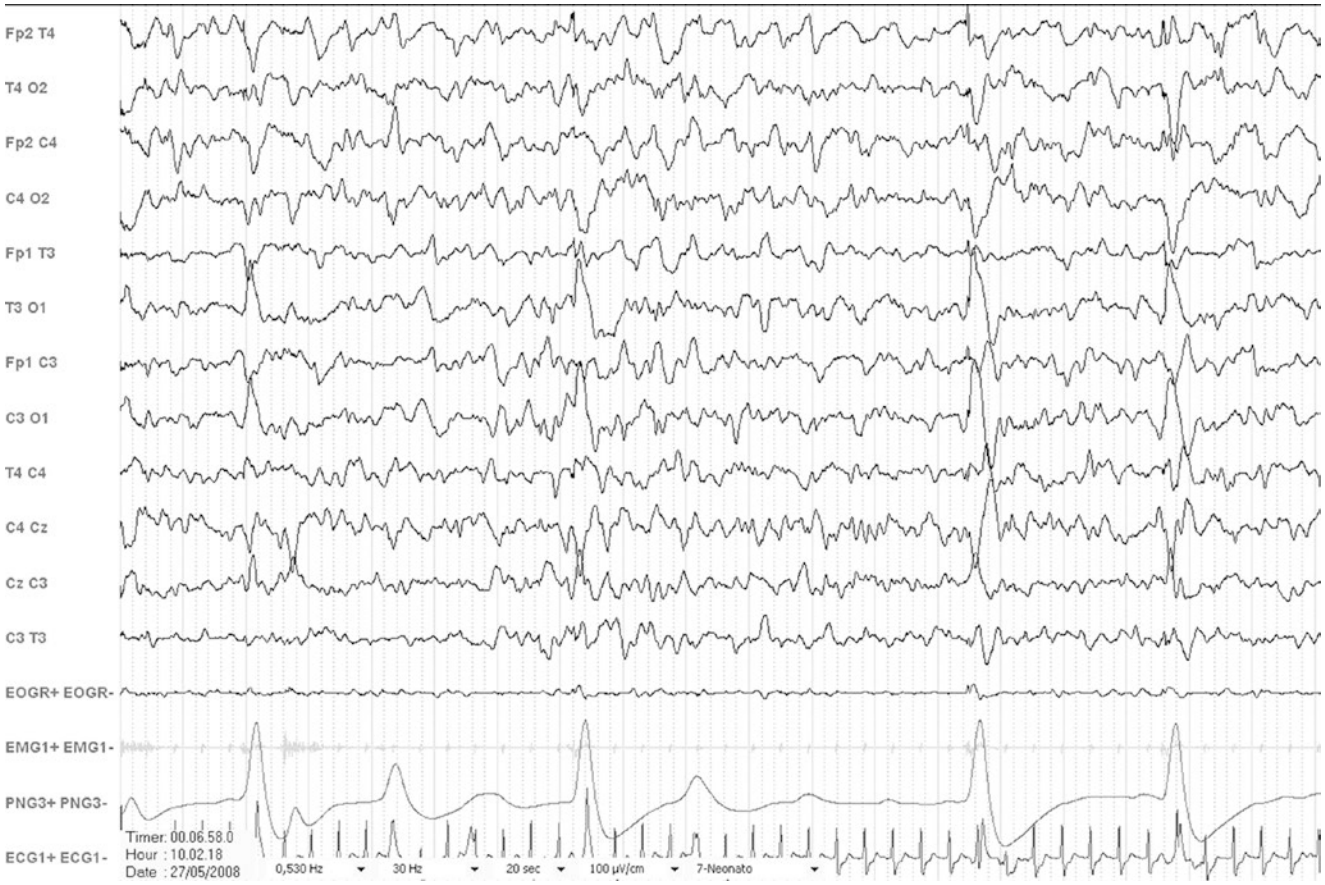

Fig. 22.18 40.6 weeks GA, 42 weeks CA (same child shown in the previous figure). After 1 week, same clinical conditions. It is shown how the superior limb muscle contraction during sleep, identified in mylohyoid muscle lead, is strictly related to an abdominal contraction (4 events in 18 s), detectable in PNG3 (abdominal respiration). A similar artifact is detected over the scalp: high-voltage negative deflection, more evident in O1, directly associated with a slight vertical deflection

22.4 The Abnormal EEG Recording: Historical References

The French school of Dreyfus-Brisac [5, 6] and Monod [7] should be acknowledged for the interest and the development of electroencephalography in newborns. Later, many other authors have tried defining and systematizing the characteristics of the EEG abnormalities. Given the practical intentions of this Handbook, should be cited above all Lombroso [8], Stockard-Pope et al. [9], Ferrari et al. [10], Mizrahi et al. [11], André et al. [12], and Hrachovy and Mizrahi [3]. There is a concordance among the authors about the opportunity to subdivide the abnormalities into four main categories:

- Abnormal features of development (Box 22.1)
- Abnormal features of the underlying background activity (Box 22.2)
- Abnormal EEG patterns/transients (Box 22.3)
- Ictal epileptic discharges (Box 22.4)

The severity of the abnormalities detected on the EEG generally correlates with the severity of neurological damage. However, the time elapsed between the clinical event and the time of recording should be considered. Indeed, the abnormalities are more significant close to the clinical event and then tend to be less evident moving away from it. Nevertheless, either their persistence, worsening, or slow regression represents a sign of severity related to the underlying brain pathology. To delineate the evolution of the abnormalities, several recordings are needed (see the following paragraph on the approach methodology to the abnormal recording).

Lombroso [8, 13] describes in detail the characteristics of the abnormal EEG features and of the ictal epileptic patterns in the preterm and in the full-term newborns. Stockard-Pope and coll. [9] provide a broad framework, with a corresponding iconography, of the four main categories, examining constantly the clinical significance of the EEG abnormalities. However, they suggest a "classification system" that seems

excessively difficult to apply; therefore, it is scarcely used in neonatal electroencephalography labs. Ferrari and coll. [10], after describing both the normal and the abnormal EEG patterns in different CAs, compared to the other authors, identify the peculiar EEG patterns subdividing them into three main categories: the first includes extremely pathological activity, the second moderately pathological activity, and the third normal or mildly abnormal activity. This classification has a clear relation with the clinical picture, thus being the tool to include the EEG features in the clinical context. In the summary table of their work, the authors highlight the different types of recordings and the different "abnormal transients" in the previously mentioned three main categories. André et al. [12] underline the need for a precise neonatal EEG terminology to achieve homogeneity and interobserver agreement in the analysis of normal and abnormal EEG recordings. Mizrahi et al. [11] and Hrachovy and Mizrahi [3] emphasize the patterns of uncertain meaning and, with respect to the background EEG activity, differentiate the generalized abnormal feature from the focal ones. In the chapter dedicated to neonatal seizures, they provide an exhaustive exposition of neonatal seizures, with a significant iconography illustrating seizures in different clinical conditions.

The interested reader is invited to refer to the abovementioned works and to the recommended references at the end of this chapter for further information.

22.5 Methodological Approach

The EEG examiner's knowledge of the "normal" features, taking into account the individual variability and the extra-neurological conditions that can modify these features, is the essential condition to face the "abnormal" EEG with its related questions. It has also been emphasized how the visual analysis of the EEG recording involves the observation and the spatial and temporal definition of specific characteristics of both the "EEG features" of the background activity and the "typical graphoelements" of each specific CA.

Once the neurological clinical condition and the behavioral state of the newborn have been delineated, the EEG allows to acquire essential information to answer the questions that together contribute to define the three fundamental points in the management of a pathological newborn: the diagnostic definition, the therapeutic approach, and the prognostic definition. Are there signs of CNS diffuse or focal injury? Are clinical or electrical seizures present? Are there any significant elements suggestive of a specific etiology? What is the effectiveness of a given therapy? When did the brain injury occur? What is the evolution of the acute event? [14].

The answer to these questions relies on the assessment of an abnormal background pattern and its relation with the CA, the lack of age-specific features, the presences of abnormalities in spatial and temporal EEG organization along with the identification of abnormal features (slow, focal, and/or diffuse), epileptic and/or non-epileptic paroxysmal abnormalities, the possible presence of ictal discharges, and finally the detection of EEG graphoelements suggestive for specific etiologies.

With respect to therapeutic behavior, the presence of specific patterns can lead to an etiological and symptomatic therapeutic treatment. In case of use of sedative drugs (midazolam, thiopental sodium, phenobarbital), the EEG characteristics allow to establish the optimal therapeutic dosage of drugs, in particular in relation to the characteristics of the ictal paroxysmal abnormalities or suppression-burst pattern. Only the EEG allows the recognition of electrical-only seizures or minimal clinical signs (i.e., electro-clinical dissociation) that might suggest therapeutic modification. In the presence of well-defined electro-clinical seizures, isolated or recurrent up to the epilepticus status, the EEG allows to evaluate the efficacy of the anticonvulsant therapy. In the hypoxic-ischemic encephalopathy, the EEG or the more commonly used amplitude-integrated EEG (aEEG) has become an important tool for the diagnosis and for the hypothermic treatment. (Discussing the aEEG characteristics is beyond the purpose of the present chapter.)

Moreover, with respect to the prognostic significance, it is only with the repetition of the EEG recordings over time, evaluating the evolution of what was found in the previous examinations that it is possible to provide some preliminary prognostic information.

Lastly, it is well known that most epileptic seizures in the neonatal period are symptomatic of an acute brain injury [2, 14]. However, in recent years, the huge expansion in genetics techniques allowed to define etiological diagnosis. Regarding the genetically determined cellular mechanisms causing nonstructural acute symptomatic neonatal seizures, three main neonatal epileptic conditions are defined: neonatal genetic epilepsies, early-onset encephalopathy, and early-onset epileptic encephalopathy [15–18, 30]. Interestingly, however, the phenotypical spectrum associated with variations in each gene can vary widely. In the majority of cases there is a spectrum of clinical manifestations, which can be associated with a wide range of phenotypic severity. For example, mutations in KCNQ2 gene have been associated with both self-limited neonatal-onset epilepsies and neonatal-onset epileptic encephalopathies [17]. Therefore, a clear-cut genotype–phenotype correlations is not always possible [16, 18].

In view of the above and according to literature [14, 19–29], it is considered useful to propose some "operational considerations."

22.5.1 EEG Recording

- It must be performed under all clinical conditions in which CNS involvement is suspected. EEG-polygraphy is essential for the definition of the behavioral states and must be individualized according to the clinical events to be documented. For the definition of the paroxysmal events, either epileptic or non-epileptic, video-EEG recording is strongly recommended. The first recording must be carried out as soon as possible and must last at least 45–60 min in the suspicion of epileptic seizures, if possible, before the anticonvulsant treatment and in hypoxic-ischemic encephalopathy in the first 6 h of life to prescribe cooling therapy.
- Long-term monitoring (24–48–72 hours) or repeated recordings in the short run are strongly suggested in the evidence of a documented or suspected status epilepticus. Moreover, also in case of subclinical or suspected seizures, it is useful to perform an EEG recording in an appropriate time in order to capture the ictal event, possibly with a video-EEG recording.
- The subsequent EEG or long-term monitoring must be performed in relation to the different peculiar clinical pictures, following the evolution of the symptoms. For the long-term prognostic definition, it is essential to evaluate clinical signs and symptoms following the acute brain injury together with the different short-term and long-term evolution of EEG patterns.

Only after the acquisition of such a methodological approach it will be possible to take into consideration the characteristics of the abnormal EEGs findings.

22.6 Essential Terminology

According to the indications of Lombroso [13], Stockard-Pope et al. [9], Ferrari et al. [10] and Mizrahi et al. [11], Andrè et al. [12], and Hrachovy et al. [3], we consider useful to report the most frequent definitions regarding the description of pathological EEG patterns.

Box 22.1: Abnormalities of the Behavioural States Organization and of the Developmental Pattern

Abnormalities of the behavioural states organization and of the developmental pattern.

Unrecognizable behavioral states: persistent absence of a recognizable sleep and waking cycle in a newborn of at least 34 weeks of CA (Figs. 22.19 and 22.20)[1].

Development of the behavioral sleep states: REM sleep state lasts 50% of the sleep cycle in a newborn at term, whereas NREM sleep state lasts about 30–40%, and the rest is occupied by indeterminate sleep. There is an intra- and interindividual variation of approximately 20–30%.

Abnormal development of the sleep-wake cycling: in the pathological cases, during NREM sleep state, the presence of an abnormal ratio between trace alternant (TA) and continuous high-voltage slow activity can be observed, with persistency of TA beyond the 7th to 8th weeks after birth; abnormalities of the onset of the REM sleep state do not bear a great clinical importance; however the presence of a REM pattern in the beginning of sleep should be carefully evaluated.

Dysmaturity (external dyschronism): electrical EEG pattern where the developmental physiological features in both sleep and wakefulness states are immature for the stated CA. A dyschronism of 3 or more weeks is suggestive of persistent brain dysfunction and is often associated with other EEG abnormalities (Figs. 22.21, 22.22, 22.23, 22.24, 22.25, 22.26, 22.27, 22.28 and 22.29).

Dysmaturity (internal dyschronism): electrical pattern where the physiological features of the NREM sleep state are immature for the stated CA and consistent with a lower CA, while the wake EEG has a normal background activity. It is considered abnormal a dyschronism of 3 or more weeks, and in this case other electrical abnormalities are usually present (Figs. 22.23–22.27).

Interhemispheric asynchrony: it is defined as pathological when the EEG activity is still asynchronous for more than 75% at a CA over 30 weeks (Figs. 22.26 and 22.27).

[1]For all the figures, the following EEG recording parameters were utilized: time base 15 mm/s, sensitivity 70/150 mcV/cm, high-pass filter 0.5/1.6 Hz, low-pass filter 30/70 Hz. Otherwise, parameters are indicated (in italics).

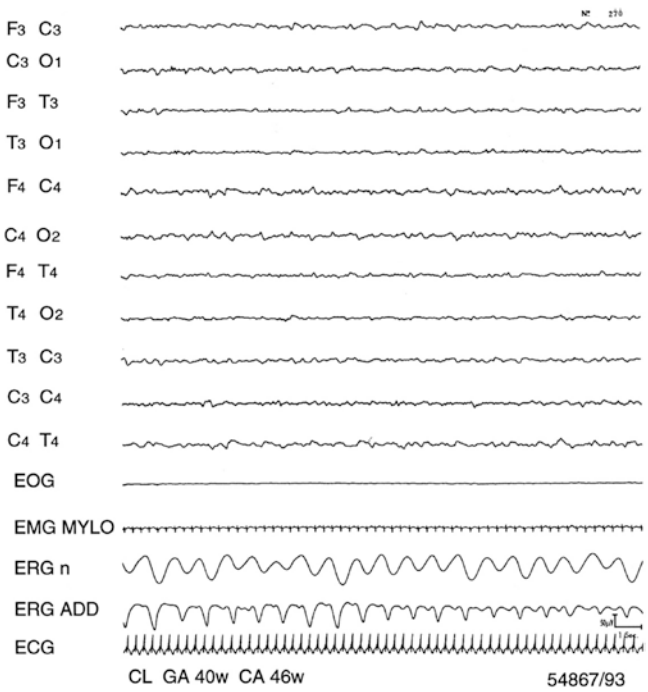

Fig. 22.19 See Fig. 22.20 caption

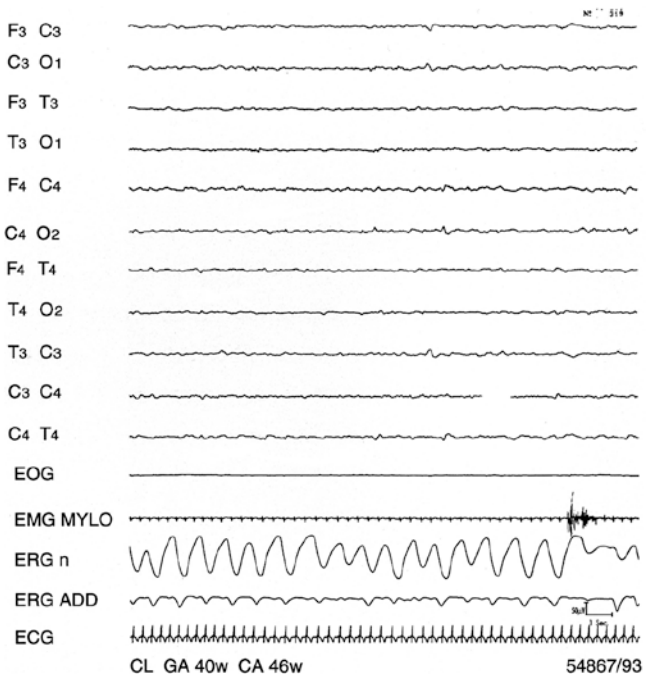

Fig. 22.20 40 weeks GA, 46 weeks CA. At 40 weeks CA, cesarean section was performed 30 h after pre-labor rupture of membranes. Maternal and newborn hyperpyrexia. Comatose newborn with AED's resistant status epilepticus, followed by recurrent seizures for a week. At 6 weeks of age **low voltage** (less than 30 mcV) **and undifferentiated tracing** throughout long-lasting EEG recording. In Fig. 22.19 polygraphic parameters are suggestive for a NREM sleep state, while those in this figure are suggestive for a REM sleep state: EEG background remains identical, undifferentiated, also during awake state. This condition is related to a **complex encephalopathy with combined etiology** (post-infective, anoxic hyschemic, intraventricular, and intraparenchymal hemorrhages). Brain MRI confirmed the etiological conclusions and documented severe and extensive lesions. Follow-up: severe neurocognitive impairment, spastic apostural tetraparesis with AED's resistant epilepsy (12 years old)

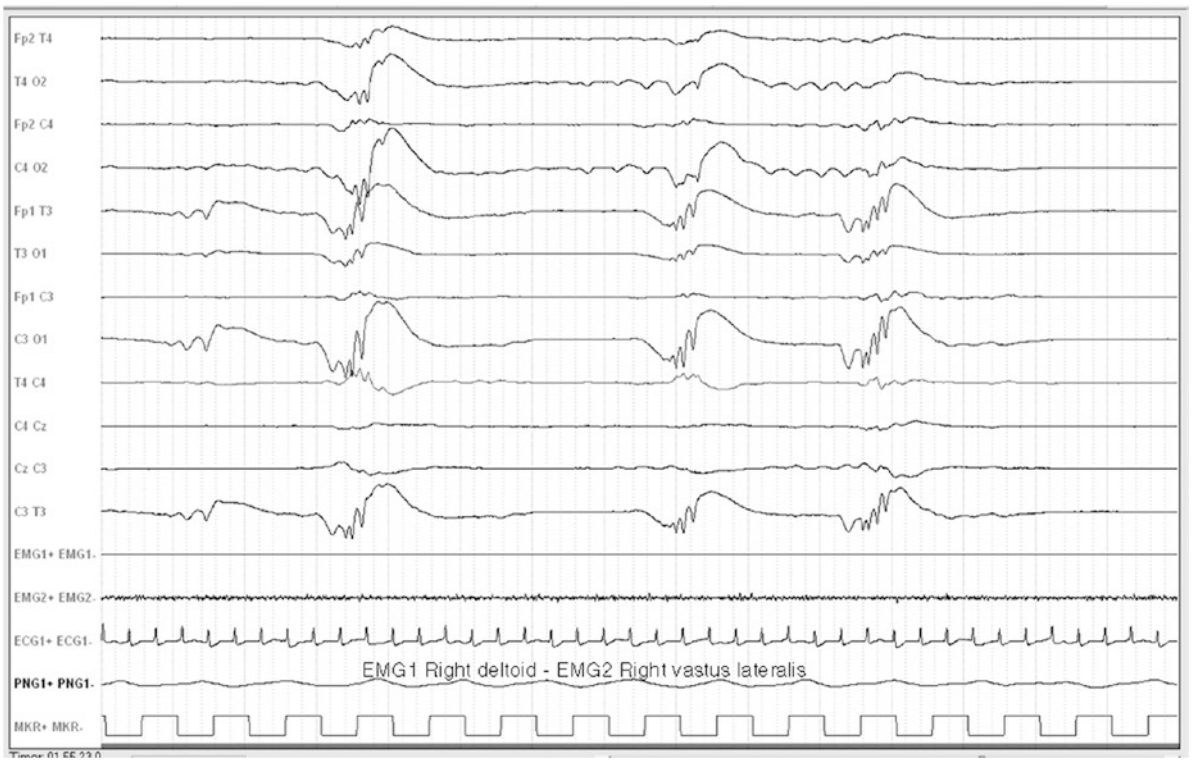

Fig. 22.21 30.3 weeks GA, 31 weeks CA. Cesarean section for pre-eclampsia. **Pathological delta brushes with discontinuous activity and temporal and occipital delta waves, synchronous on the two sides, with superimposed theta activity**. Follow-up: moderate motor and intellectual impairment (22 months old)

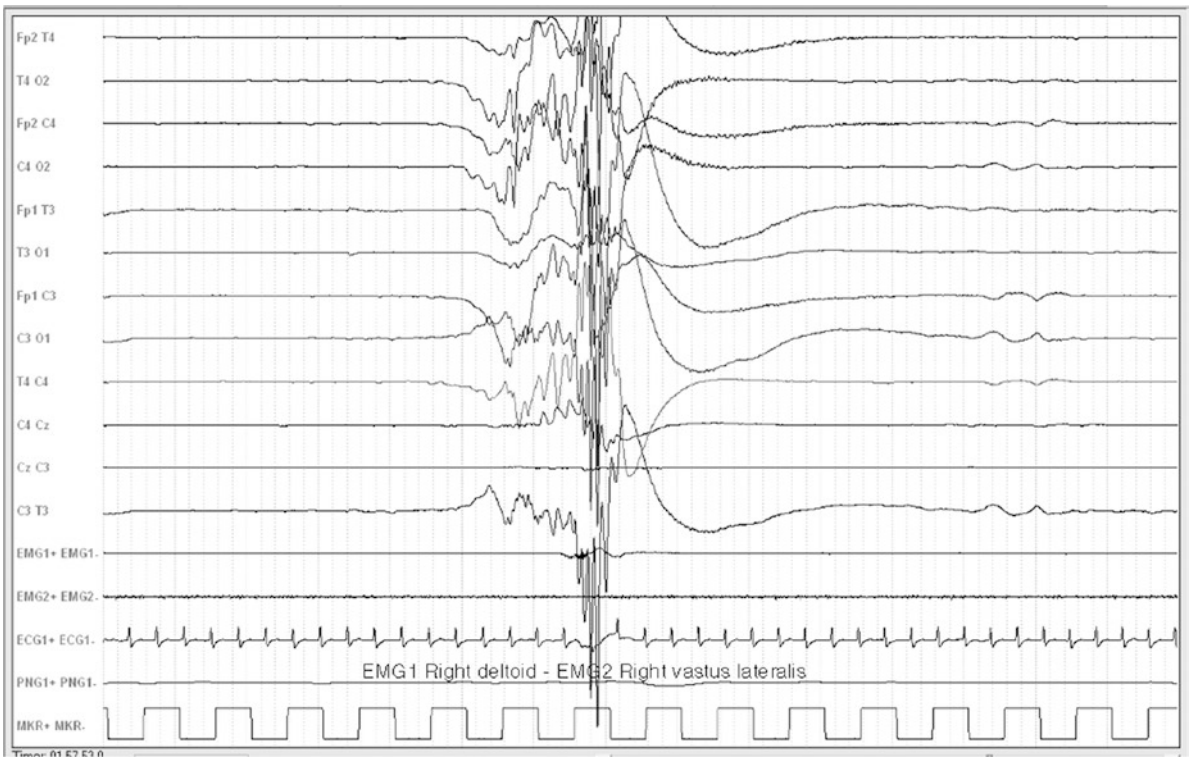

Fig. 22.22 28 weeks GA, 28.6 weeks CA. Twin pregnancy, pre-labor rupture of membranes. **External dyschronism**. During quiet sleep, discontinuous background activity **with high-amplitude delta wave superimposed by rapid and spiky rhythms. The burst begins with theta activity and is followed by very high-voltage very slow wave transient**. Synchronous low-voltage delta activity on the central regions is seen in the interburst period. Follow-up: normal brain ultrasound; normal psychomotor development (8 months old)

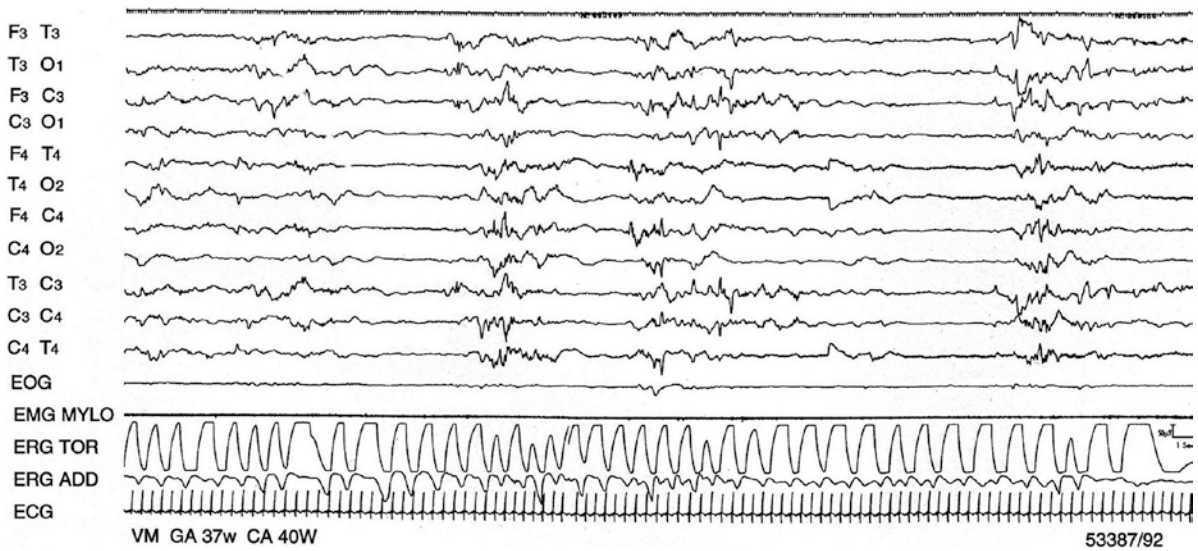

Fig. 22.23 37.6 weeks GA, 40 weeks CA. Pregnancy not monitored. Normal delivery at 37.6 weeks. Hypotonia and reduced alertness in the first 3 weeks of life. In the first week, the EEG (not shown) is characterized by immature pattern for the reported CA in all states of sleep and wakefulness. At 40 weeks CA in tracé alternant sleep, the bursts are rich in sharp elements, although exceedingly asynchronous for age. Interburst intervals have significant low voltage. **External dyschronism**

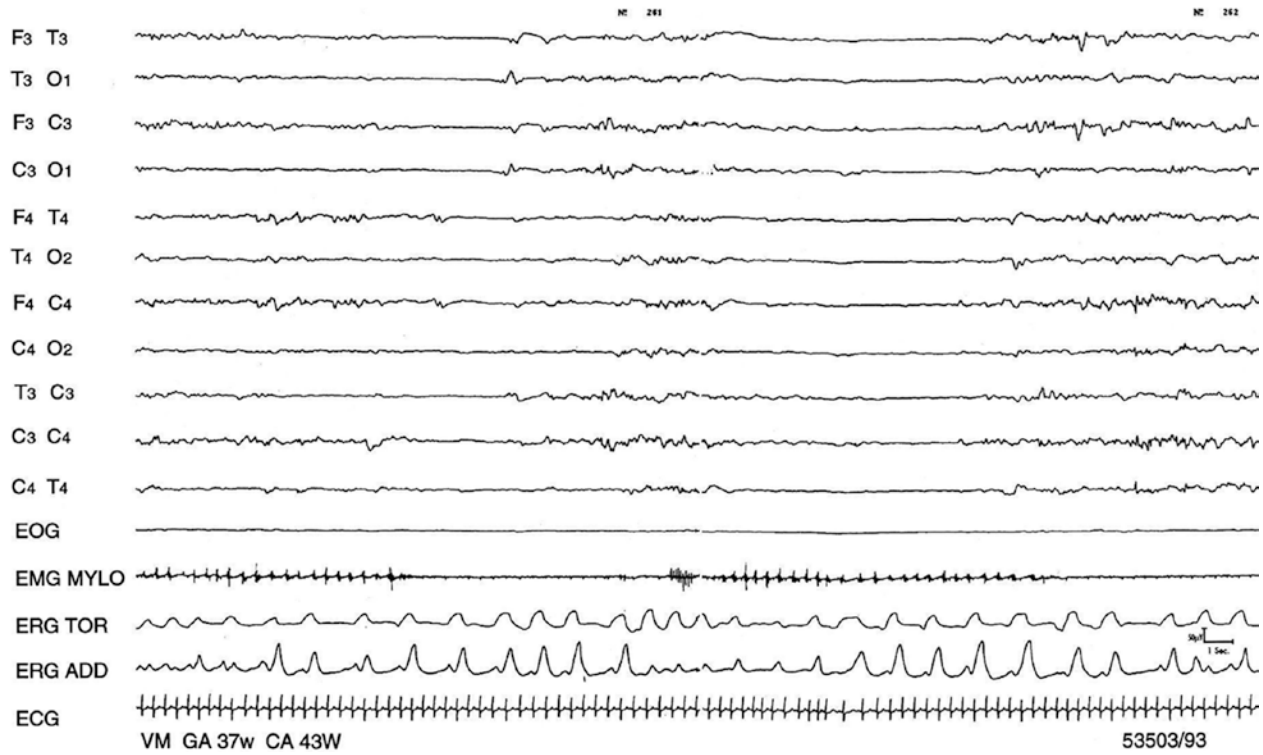

Fig. 22.24 37.6 weeks GA, 43 weeks CA (same child as the previous figure). Progressive decline of reactivity and spontaneous motility. Three weeks later in quiet sleep, significant decrease of burst amplitude and increase of low-voltage interburst intervals. The external dyschronism is evolving to a **low voltage depressed background activity** (undifferentiated EEG). Brain MRI: cortical and subcortical atrophy, bilateral lesions of white matter, result of **prenatal chronic hypoxia**. Follow-up: at 4 months West syndrome, severe neurocognitive impairment

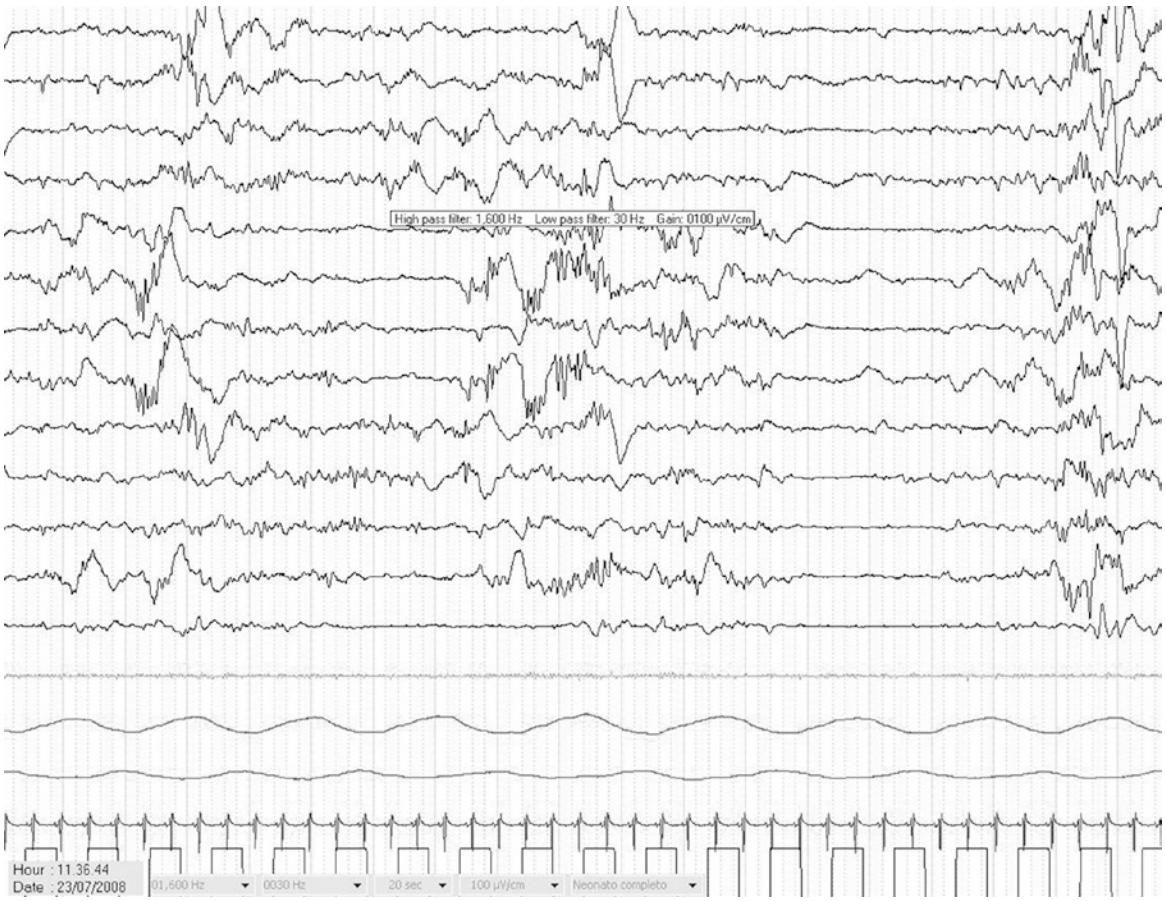

Fig. 22.25 36.6 weeks GA, 37.4 weeks CA. Uneventful pregnancy and delivery. On the 5th day of life prolonged (non-epileptic) cyanotic event. In quiet sleep asynchronous tracé alternant pattern, persistence of delta brushes and bursts with exceedingly sharp grapho-elements, and low-voltage interburst intervals. Dysmaturity (**internal dyschronism**). Normal cerebral ultrasound. Follow-up: normal neurodevelopment at 4 months of age

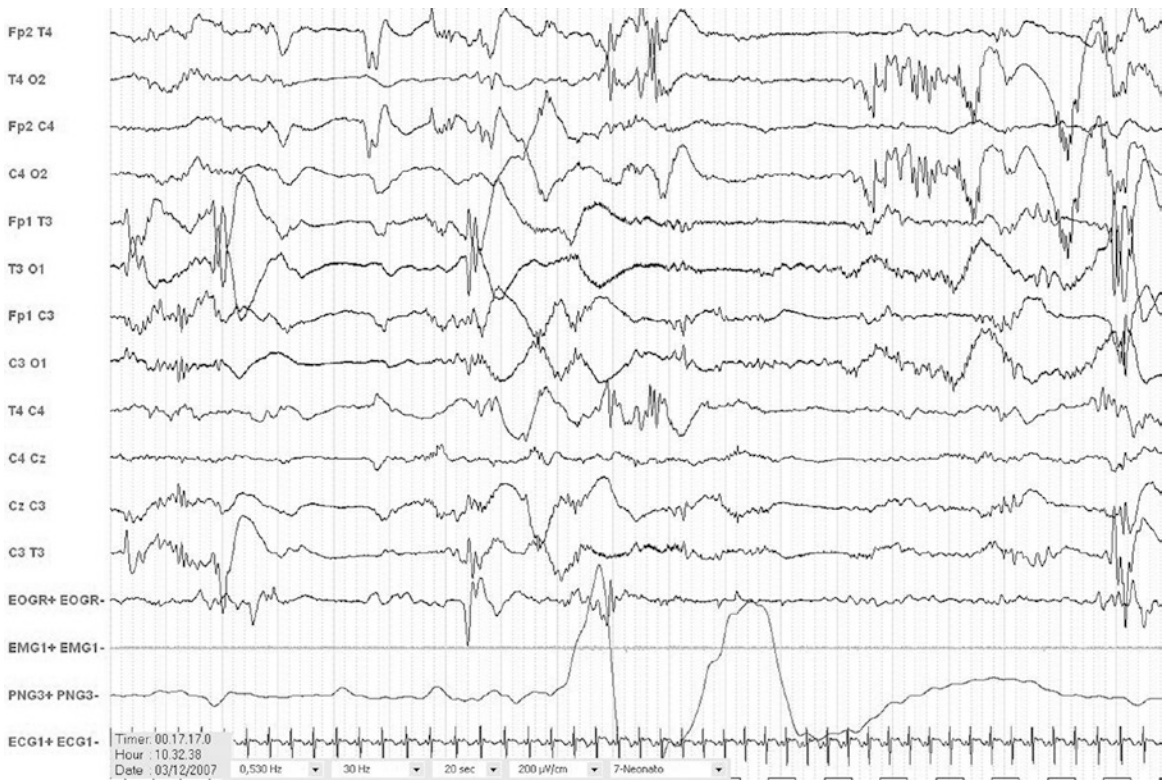

Fig. 22.26 See Fig. 22.27 caption

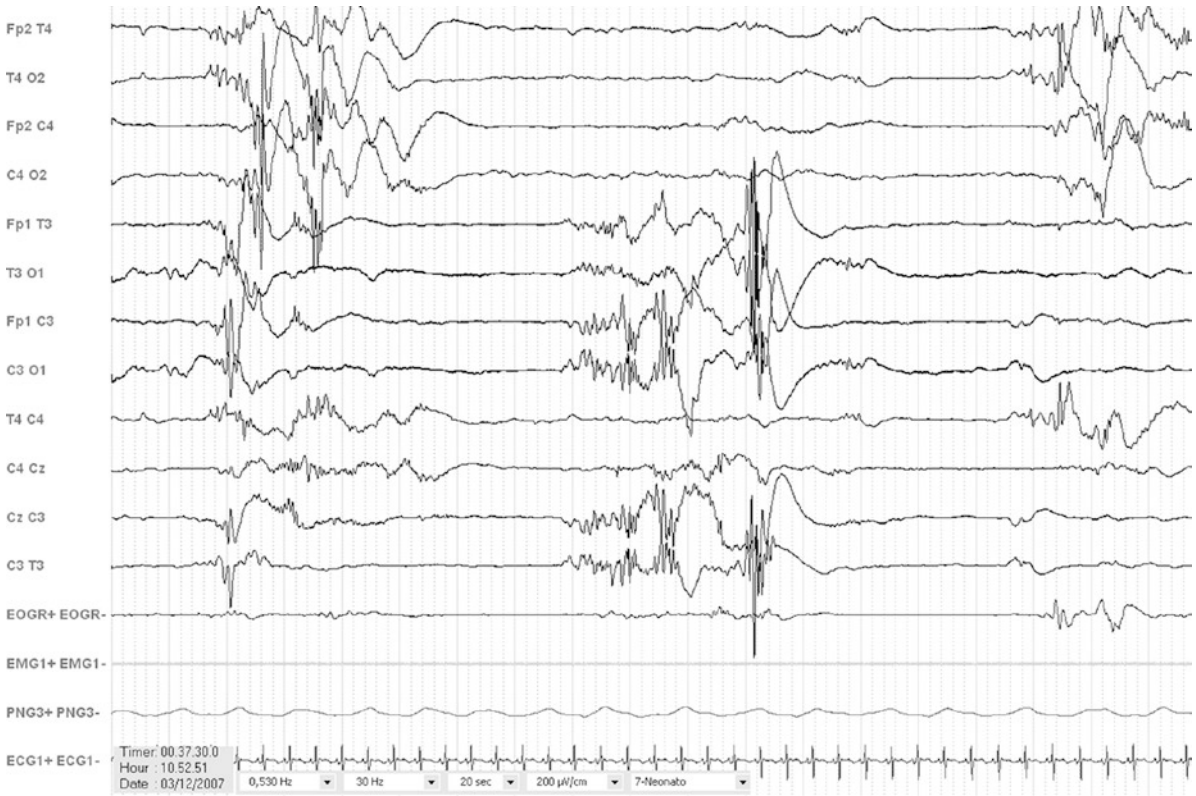

Fig. 22.27a 28 weeks GA, 32 weeks CA. **Intraventricular hemorrhage and tetraventricular hydrocephalus** occurring 5 days after birth. The newborn is lethargic. At 4 weeks of life (Fig. 22.26), active sleep with significant **interhemispheric asynchrony** of electrical activity and of inactive intervals. Multifocal spikes and polyspike-slow waves with an amplitude of 200–600 mcV, predominant in left and right temporal region. In Fig. 22.27 quiet sleep with substantial increase of inactive segments and **interhemispheric asynchrony**. Abnormal discharges with enhanced amplitude. The tracing can be defined as dysmature (**external dyschronism**), but it is highly suggestive of a multifocal injuries in consideration of discharges strictly focal and repetitive in the temporal regions. Brain MRI: tetraventricular hydrocephalus. Follow-up: ventriculoperitoneal shunt, normal electro-clinical conditions at 11 months

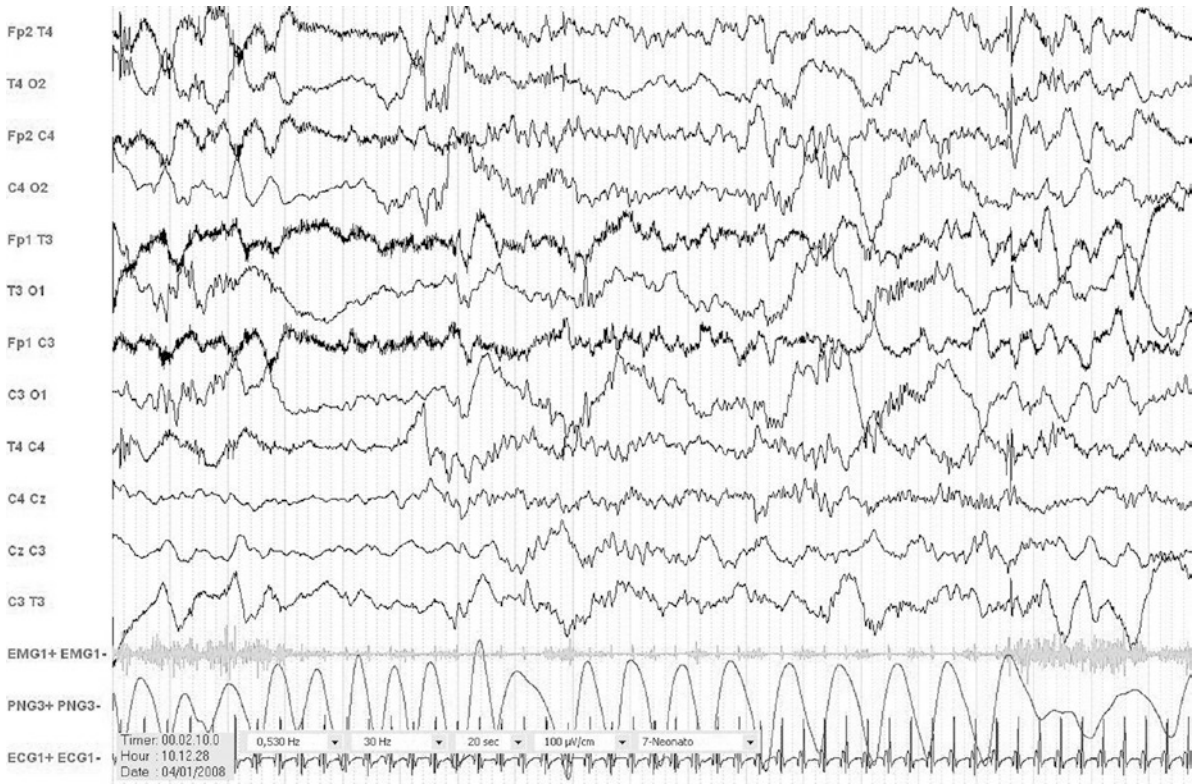

Fig. 22.27b 27 weeks GA, 40.4 weeks CA. **Prematurity** with low birth weight 517 g (small for gestational age—SGA). Cerebral ultrasound: persistent periventricular parenchymal echogenicity. Irritability and wake/sleep cycle alteration. Awake EEG shows, besides the associated muscle activity, several artifacts, diffuse and transient (4 s) attenuation of the background, **external dischronism** (present also during quite sleep with prolonged bilateral asynchronous flattening of the background)

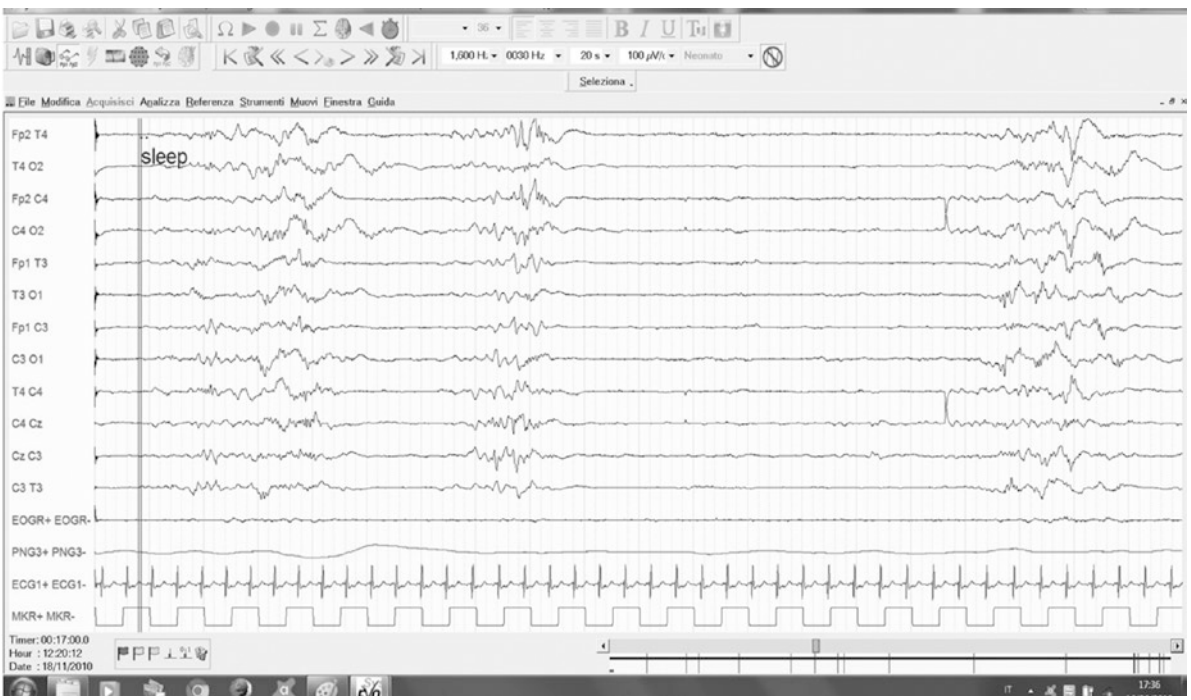

Fig. 22.28 38 weeks GA, 38.5 weeks CA. Pregnancy complicated by polyhydramnios from the 32nd week GA. Uneventful spontaneous delivery. The newborn is hypotonic and hyporeactive, with feeding difficulties. During quite sleep, the **EEG background is quite discontinuous** with bursts (3–8 s) characterized by delta-theta high-voltage and beta slow-voltage activities with intermixed sharp waves asymmetrical between the two hemispheres separated by periods (3–10 s) of marked generalized voltage attenuation

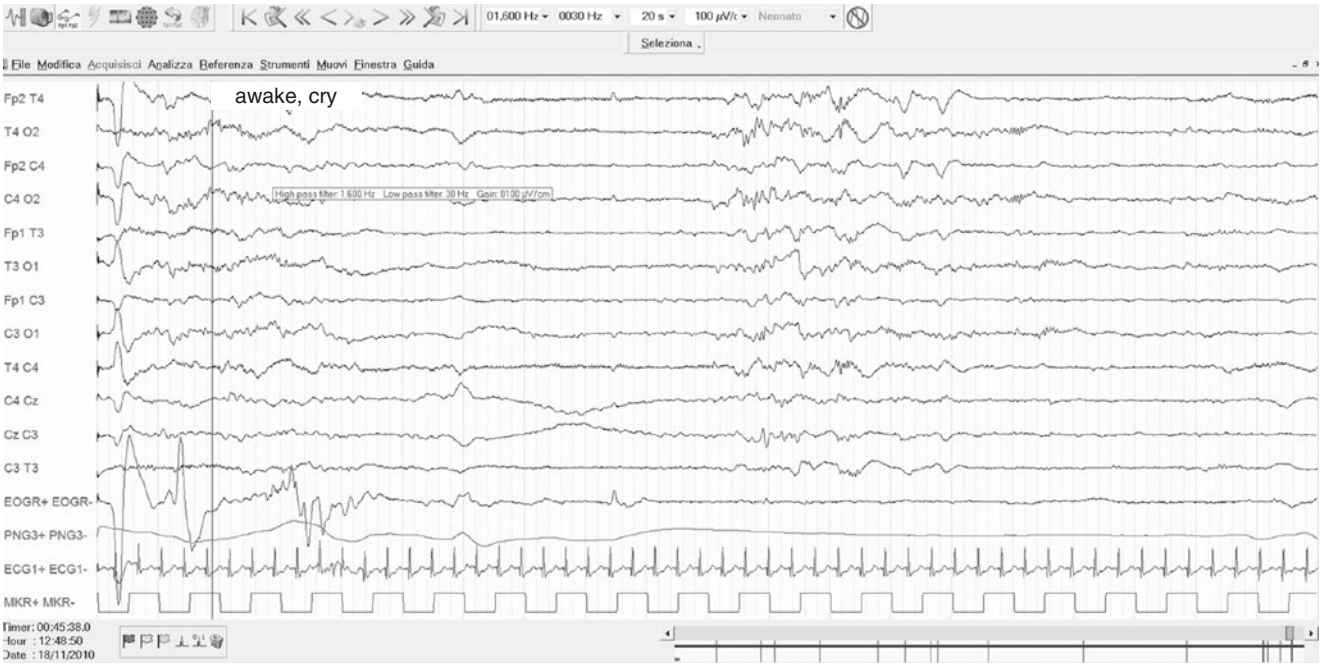

Fig. 22.29 Same newborn and same recording of Fig. 22.28. While awake, the baby is crying with open eyes. The **EEG pattern is discontinuous** and similar to what shown during quite sleep; however the bursts are longer. CGH array disclosed a 2.4 Mb de novo deletion in 9q34.11, containing STXBP1 and SPTAN1. **STXBP1 and SPTAN1 neonatal encephalopathy**. Follow-up: epileptic spasms at 2 months, easily controlled by GVG. Severe neurocognitive impairment, without epilepsy at 4 years

Box 22.2: Background EEG Activity Abnormalities

Inactive or isoelectric EEG: cerebral activity constantly lower than 5 mcV and unreactive to somatosensory stimuli (Figs. 22.30 and 22.31).

Suppression-burst EEG pattern: characterized by low-voltage intervals of inactivity (voltage <5 mcV) of variable length, usually longer than 10 s, separated by bursts of high-amplitude (rarely of low voltage) activity of 0.5 up to 10 s in duration. This pattern (Figs. 22.32, 22.33, 22.34, 22.35, 22.36, 22.37 and 22.38) must be distinguished from the discontinuous EEG pattern of the very preterm newborn. In some cases there is a continuum between very discontinuous EEG pattern and suppression-burst EEG pattern (Figs. 22.28, 22.29, 22.39, 22.40, and 22.41).

Persistent low-voltage activity (undifferentiated): EEG activity constantly between 5 mcV and 30 mcV; usually the voltages are modestly higher in the active sleep state compared to the wakefulness and the quiet sleep state (*rapid eye movements*) (Figs. 22.19 and 22.20).

Persistent asymmetry: persistent asymmetry of voltage higher than 50% between homologous regions of the two hemispheres or clear asymmetry of background features between the two hemispheres in all behavioral states: the typical physiological EEG transients of each conceptional week are either reduced or absent in the hemisphere with the lowest activity (Figs. 22.42, 22.43 and 22.44).

Diffuse delta activity: persistent and diffuse high-amplitude delta waves, scarcely reactive to external stimuli.

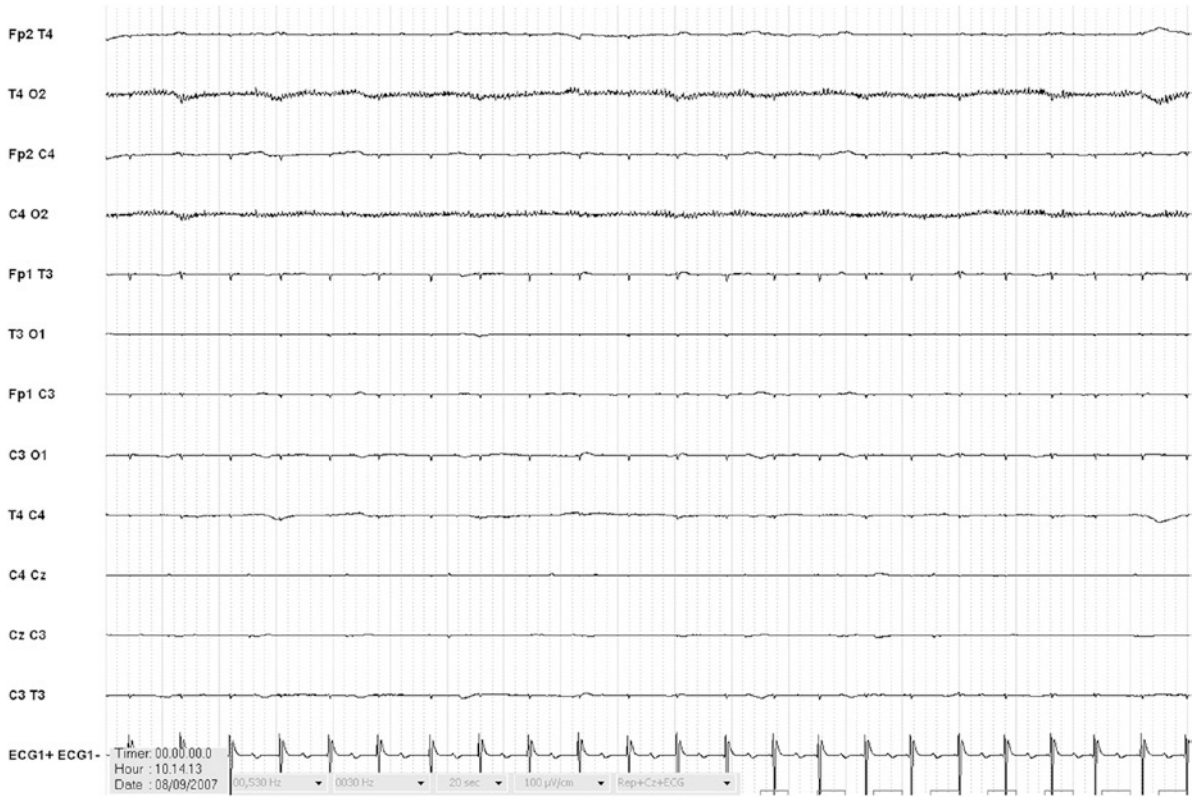

Fig. 22.30 40 weeks GA; 40 weeks CA. Uneventful pregnancy, spontaneous delivery, with shoulder engagement in the expulsive phase **>acute transitory hypoxic ischemic encephalopathy**. Birth weight gr 3770, Apgar score 1-3-5 (at 1′-5′-10′), pH 6.8, BE-22 mmol/L. At 10 h after birth, the newborn is still comatose, unreactive, with severe hypotonia and absence of spontaneous motility, mechanically ventilated in hypothermia treatment. **Inactive tracing** (amplitude constantly less than 5 mcV), not reactive to stimulation. In the first 12 h isolated symptomatic epileptic seizures. Normal brain MRI at 7 and 30 days. Follow-up: normal psychomotor development associated with brachial plexus palsy

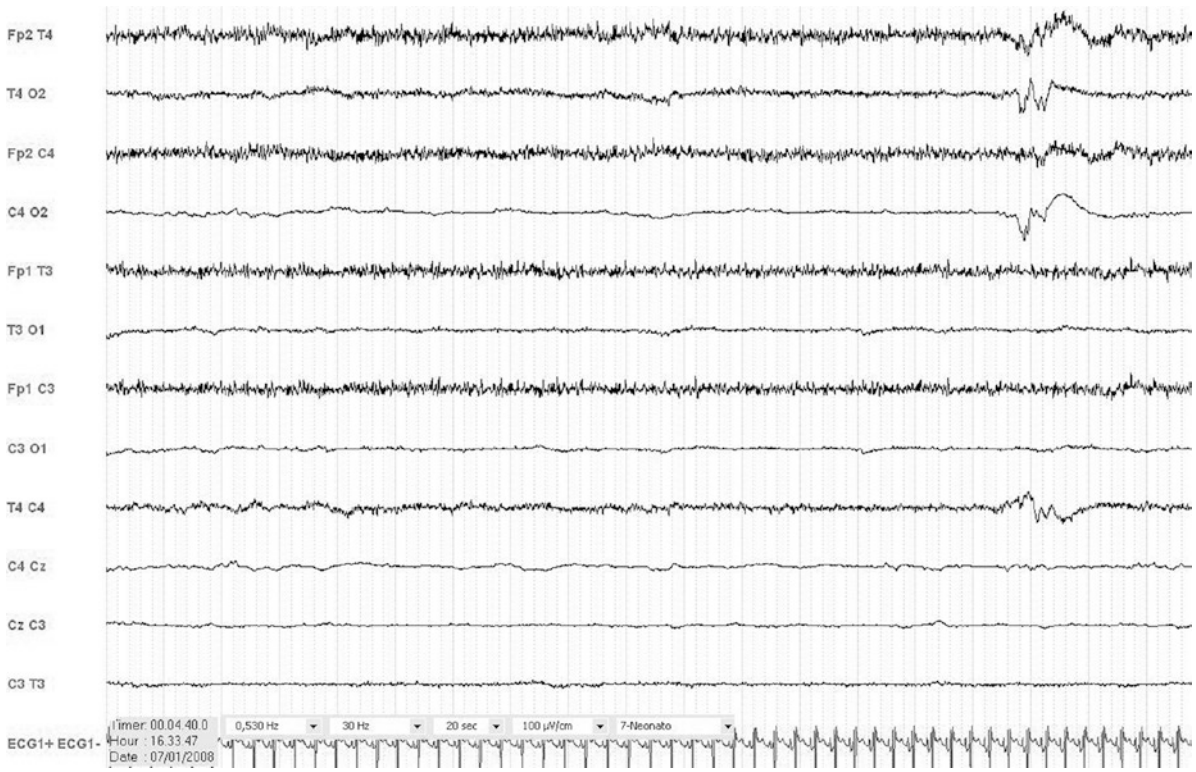

Fig. 22.31 Same case of Figs. 22.66 and 22.41 weeks CA. Three days after the above examination a prolonged heart arrest occurred. Unreactive coma, mechanically ventilated. **Inactive tracing** (amplitude constantly less than 5 mcV), not reactive to stimulation. Few isolated erratic delta and sub-delta slow waves (40–80 mcV) rarely occur, intermingled with slow spikes (up to 80 mcV) or short runs of sharpened theta activity. **Post-anoxic coma**. The next day the newborn died

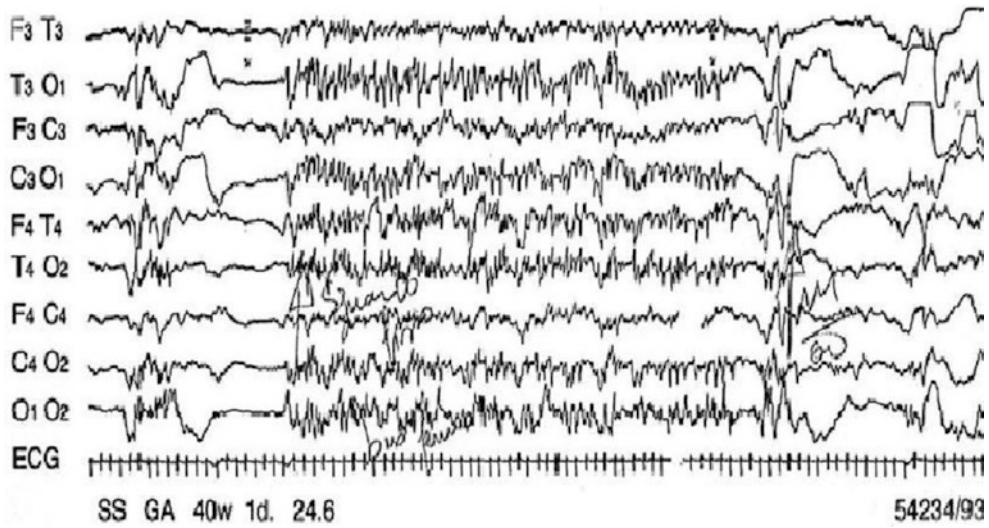

Fig. 22.32 40 weeks GA. Uneventful pregnancy and delivery. On the 1st day, the newborn is lethargic and hyporeactive. Atypical suppression-burst EEG pattern (1–3 s inactive periods intermingled with 1–2 s bursts of slow waves, spike, and sharp-wave activity, up to 250 mcV). In the middle of the figure, **electrical seizure with fast activity that arises from the posterior region, clinically associated with staring**. **Neonatal epileptic encephalopathy B6 deficiency related**. Vit B6 150 mg EV therapy led to seizures control and disappearance of suppression-burst pattern (not shown). Follow-up: mild neurocognitive impairment, normal brain MRI. Remission of epilepsy with chronic B6 therapy (8 years old)

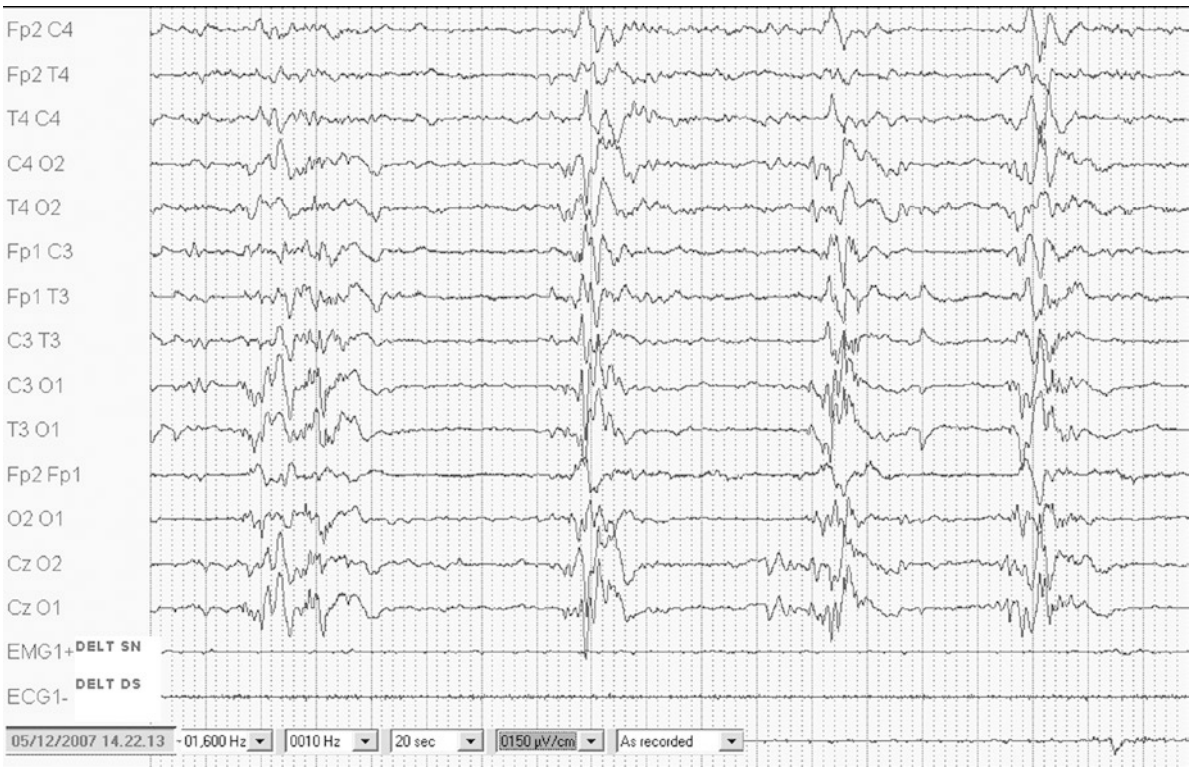

Fig. 22.33 40 weeks GA, 41.4 weeks CA. Uneventful pregnancy and delivery. Recurrent focal right clonic seizures and series of focal spasms from the 2nd day of life, resistant to B6, LZP, and PB IV. In between the seizures, the newborn is hypotonic and hyporeactive. **Asymmetrical suppression-burst** EEG pattern with high-voltage spikes and poly-spikes, more evident in left regions. **Neonatal encephalopathy related to repetitive seizure recurrence.** Seizures were controlled by GVG (105 mg/kg/die) therapy, with disappearance of the suppression-burst pattern. Focal clonic right seizures recurred at 1 year old; the brain MRI showed a dysplastic left parieto-occipital lesion. Follow-up: slow progressive neurocognitive impairment associated with AED's resistant epilepsy (12 months old). (Dott. ML Carpanelli courtesy)

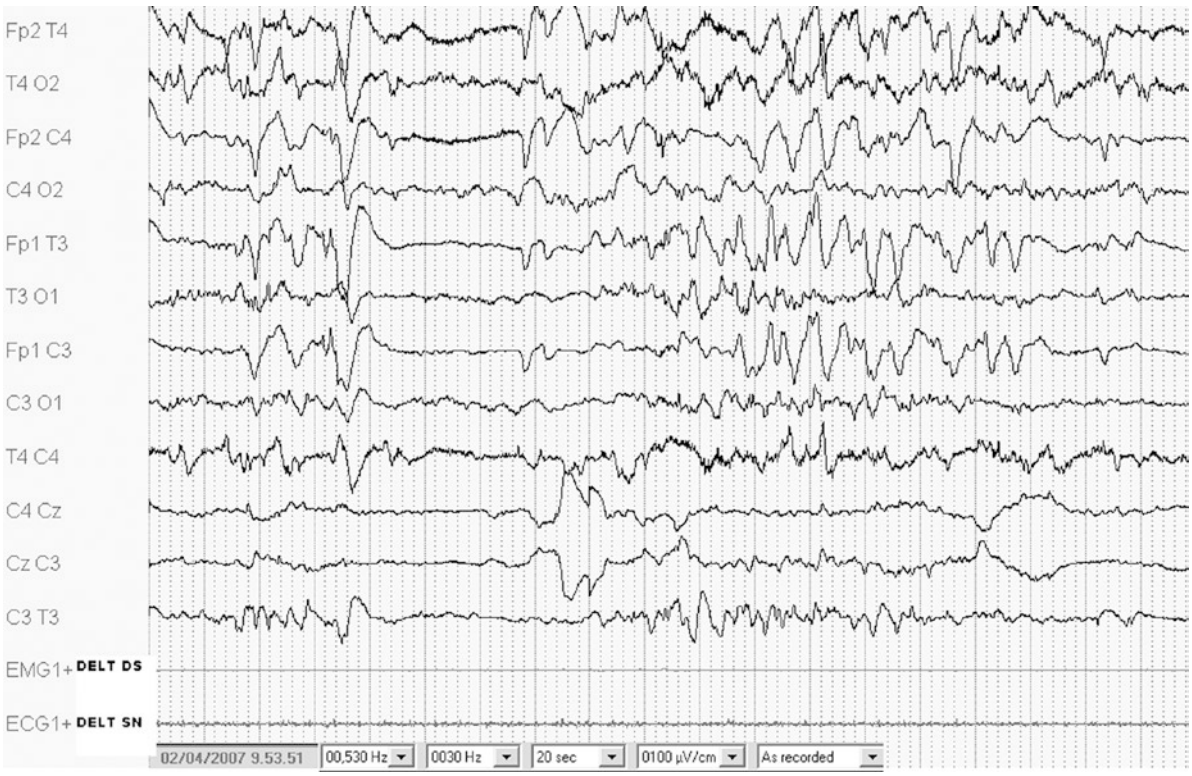

Fig. 22.34 See Fig. 22.35 caption

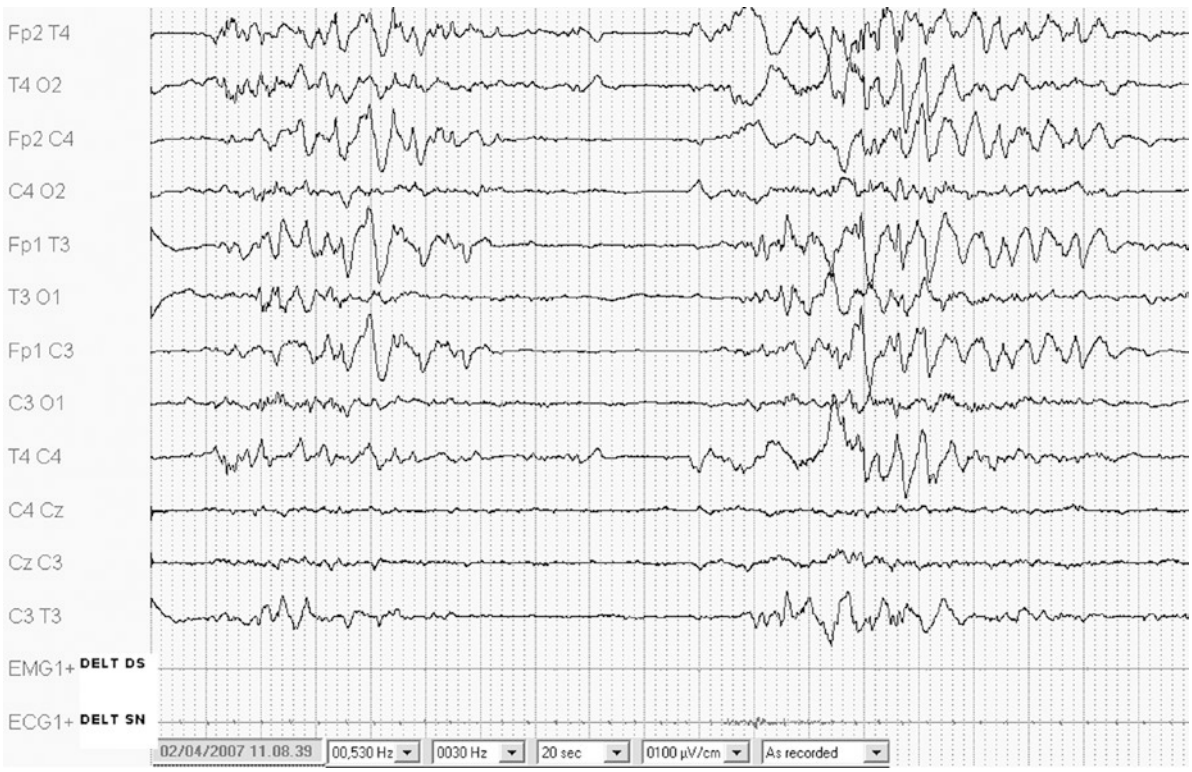

Fig. 22.35 40 weeks GA. Decrease fetal movements starting the day before delivery in an otherwise uneventful pregnancy. Acute hypoxia lasting a minimum of 24 h. Asphyxia at birth. Recurrent seizures in the first 13 days. On the 21st day of life, during PB therapy, **suppression-burst** EEG pattern: interburst bilateral intervals of 3–5 s, "inactive" (below 5–10 mcV), are intermingled with bilateral 4–10 s bursts of delta sharp slow waves mixed with spikes, up to 300 mcV. In wakefulness (Fig. 22.34) compared to sleep (Fig. 22.35), interburst intervals are shorter, and burst activity is longer; however the suppression-burst pattern is unchanged throughout the recording. **Post-anoxic neonatal encephalopathy with suppression- burst.** Brain MRI at 7 and 25 days of life: diffuse cortical-subcortical lesions due to anoxic-ischemic damage. Follow-up: West syndrome at 3 months with severe neurocognitive impairment (12 months old)

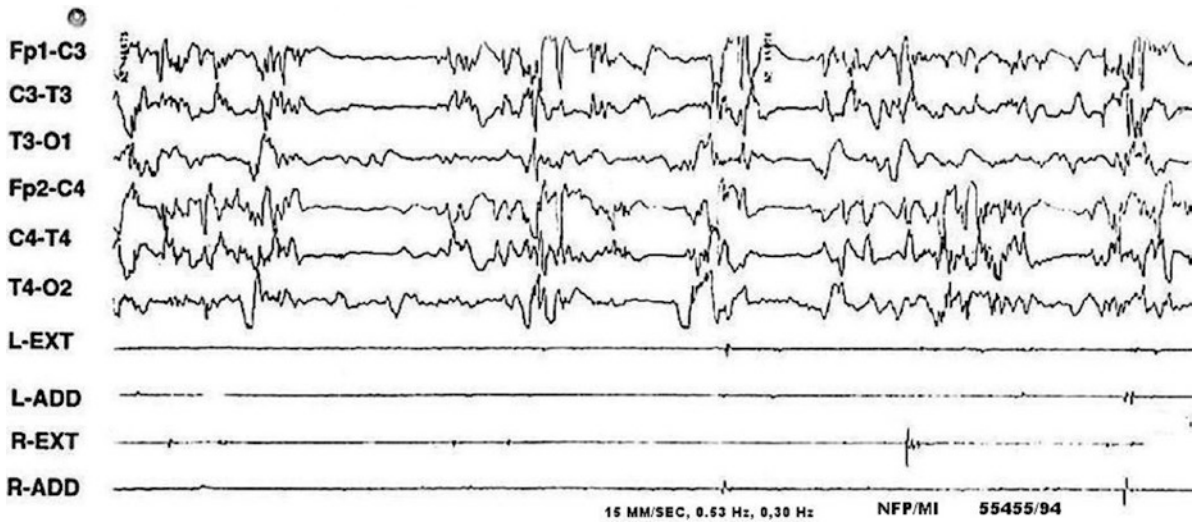

Fig. 22.36 38.4 weeks GA, 40 weeks CA. Uneventful pregnancy and delivery. In the 1st day of life, the newborn is lethargic and hyporeactive. Myoclonic jerks and spasms are referred. On the 9th day **asymmetric/asynchronous suppression-burst pattern**: 2–5 s inactive intervals are intermingled with bilateral 2–5 s asynchronous bursts, with delta and theta broad slow wave activity, up to 350 mcV, mixed with spikes and sharp waves. The bursts appear generally asynchronous between the two hemispheres, and the electrical activity within the bursts is consistently asynchronous. The polygraphy documents the presence of non-epileptic erratic myoclonies. **Early myoclonic encephalopathy due to non-ketotic hyperglycinemia**. Normal brain MRI, hyperammonemia, and high glycine levels both in blood and cerebrospinal fluid. Follow-up: tonic epileptic spasms and severe neurocognitive impairment in the first 3 months followed by continuous non-epileptic segmental erratic myoclonus. Died at 16 years old

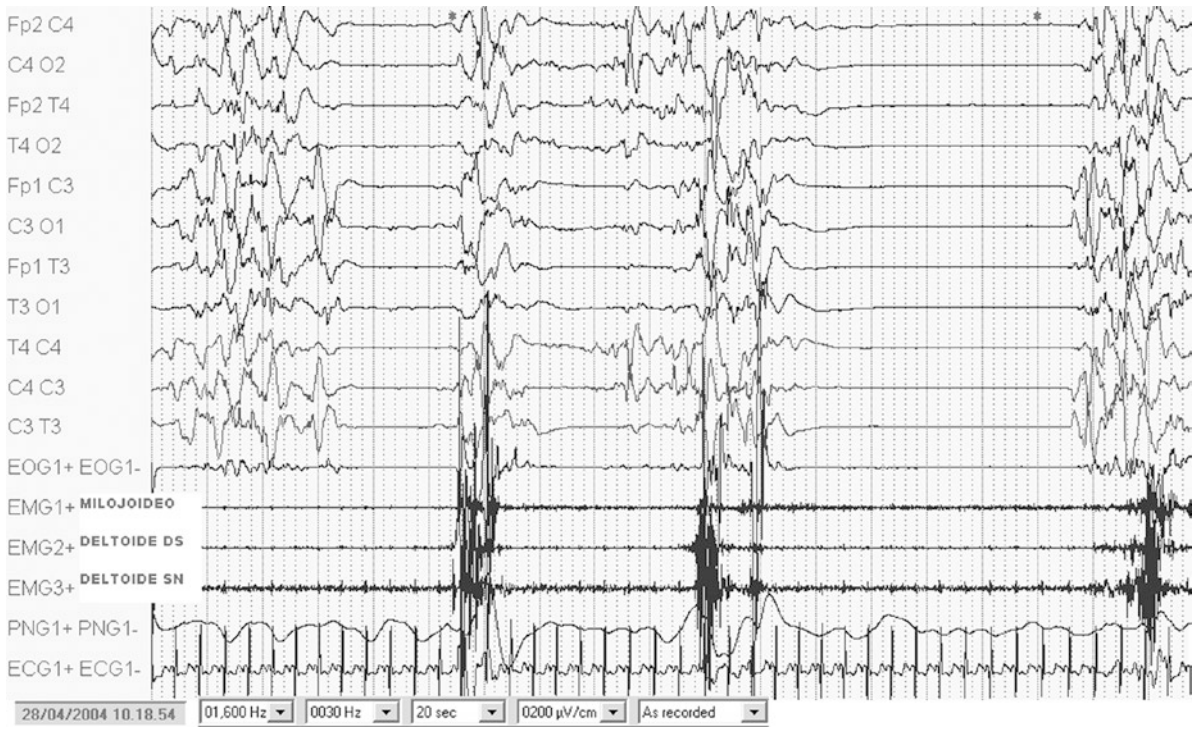

Fig. 22.37 39 weeks GA, 42 weeks CA. Uneventful pregnancy and delivery. Since the 1st day of life, the newborn is hypotonic and hyporeactive with spasms, isolated and in sequence tonic spasms, bilateral independent focal motor clonic seizures, resistant to DZP, PB, and PHT. At 21 days of life, **suppression-burst pattern with undifferentiated trace in wakefulness and sleep**. Two to five seconds flat traces (less than 10 mcV) are regularly interspersed with 2–5 s bilateral bursts of slow waves, spikes, and polyspike-slow wave complexes, up to 400 mcV. The bursts are often associated with clinic spasms and tonic spasms (recorded in polygraphy). **Early infantile epileptic encephalopathy (EIEE)**, presumed genetic in nature (Brain MRI, blood and urinary metabolic screening were normal). Follow-up: AED's resistant epilepsy > West syndrome > Lennox Gastaut syndrome with severe neurocognitive impairment (36 months old)

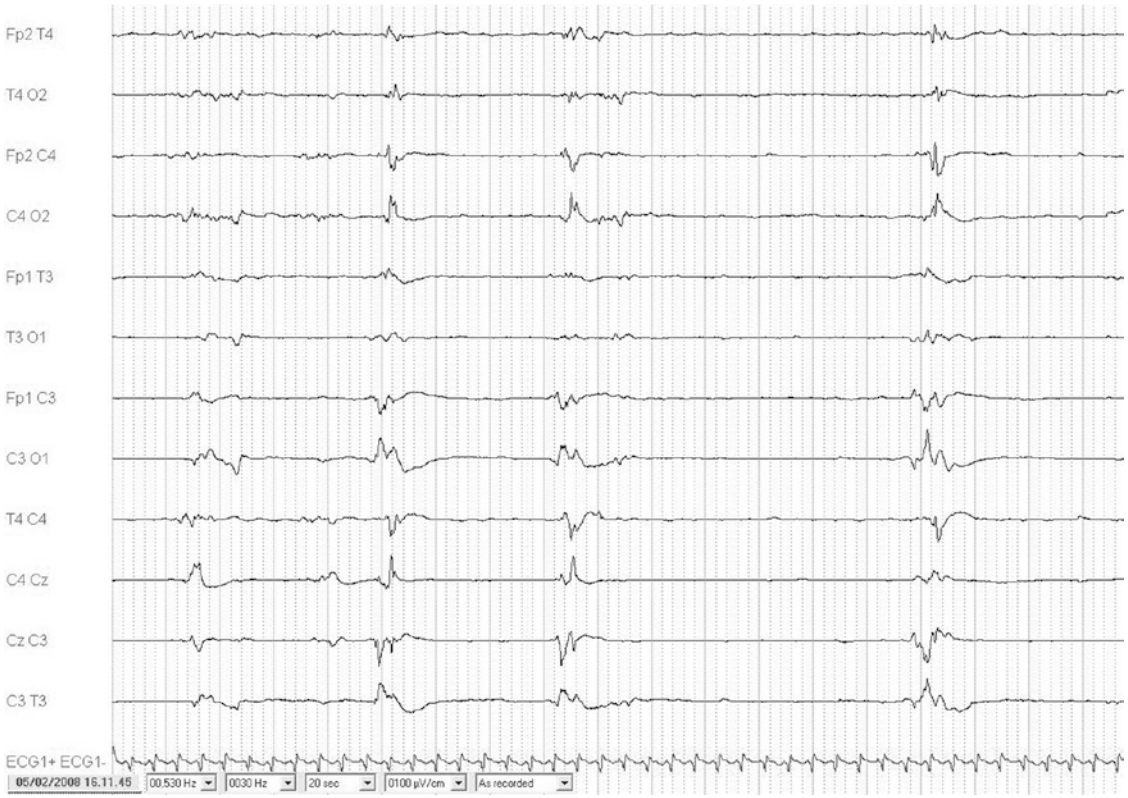

Fig. 22.38 40 weeks GA, 43.3 weeks CA. Uneventful pregnancy and delivery. At 22 days of life ***Streptococcus beta-haemolyticus*** **type B encephalitis associated with convulsive > electrical status epilepticus. Induced thiopental sodium coma with infraclinical multifocal recurrent seizures with electro-clinical dissociation and severely abnormal background activity**. Follow-up: severe neurocognitive impairment > West syndrome at 6 months > developmental encephalopathy with AED's resistant epilepsy > died at 3 years old. At 24 days of life: **suppression-burst EEG pattern** during thiopental sodium therapy with 5 mg/kg/h: 2–5 s flat periods (less than 10 mcV) are regularly intermingled with 2–5 s bilateral short (1–2 s) bursts of theta and/or delta slow waves, with superimposed spikes and/or polyspikes high as 50–150 mcV. Slow wave complexes, up to 400 mcV

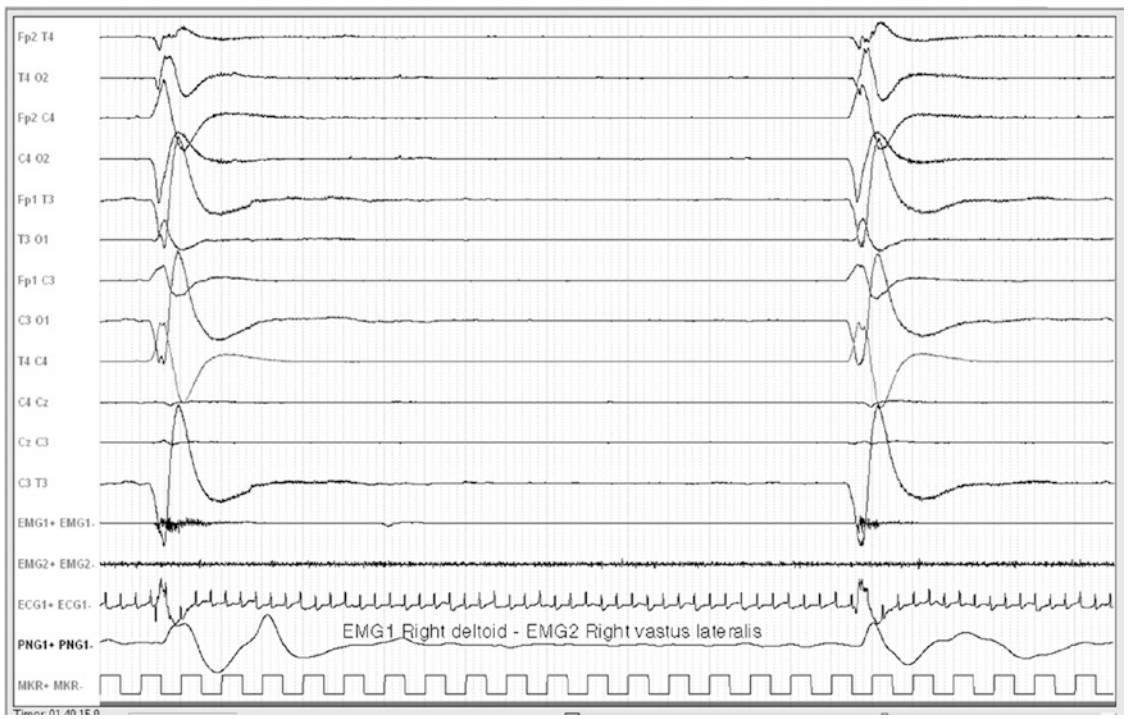

Fig. 22.39 26 weeks GA; 26.3 weeks CA. In the 2nd day of life **bilateral intraventricular hemorrhage** of severe degree. **Pathological discontinuous background activity with periodic high amplitude, biphasic delta waves with a smooth and acute shape**. Interburst intervals are flat, without electrical activity. *Time base: 10 mm/s.* Follow-up: mild intellectual disability, spastic diplegia (5 years old)

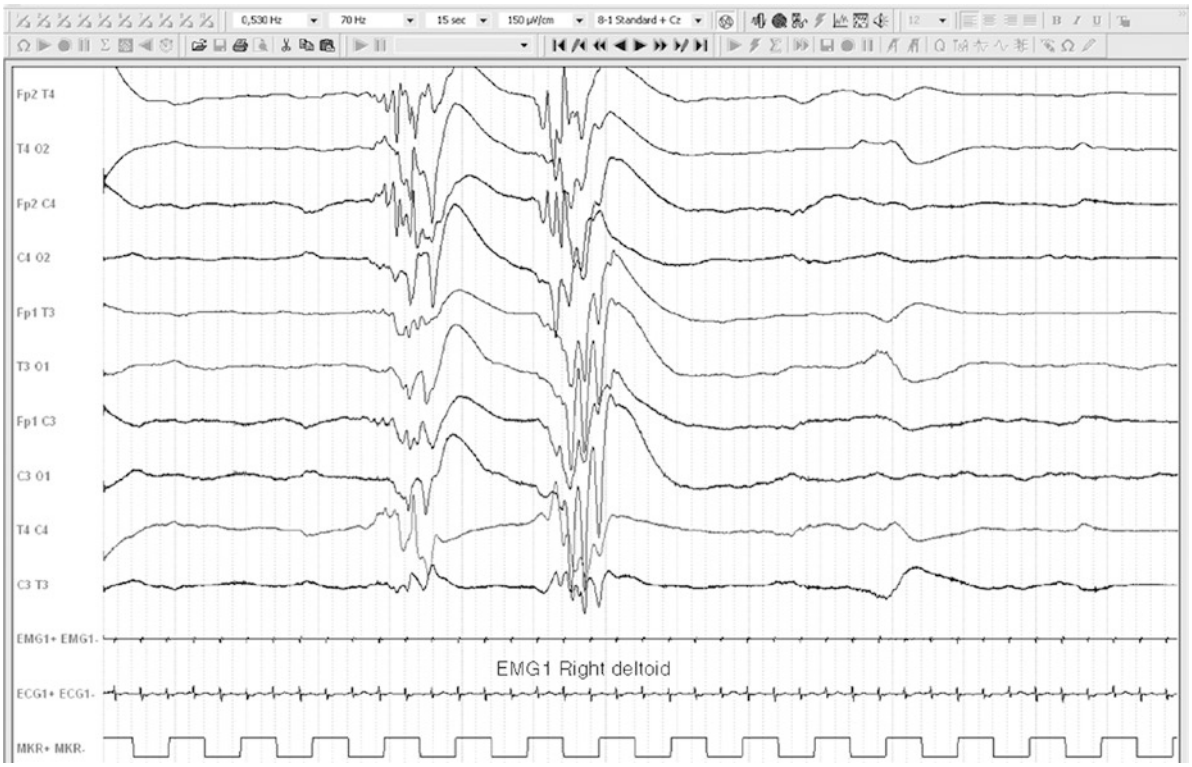

Fig. 22.40 26 weeks GA; 26.3 weeks CA. Uneventful pregnancy, prelabor rupture of membranes with caesarian section. **Bilateral intraventricular hemorrhage**. Diffuse, high-voltage theta bursts. **Pathological discontinuous tracing**. The bursts are followed by high-voltage very slow wave transients**.** The interburst interval is variable. Follow-up: mild intellectual disability with minimal motor impairment (3 years old)

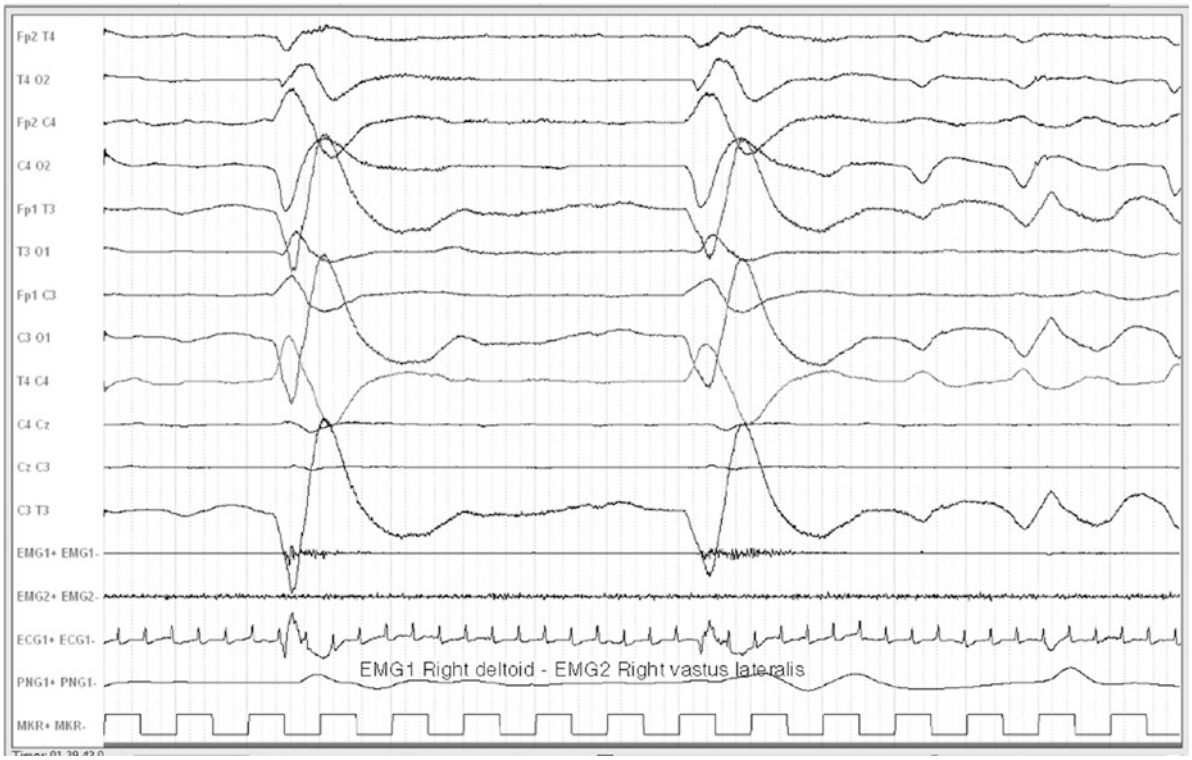

Fig. 22.41 26.4 weeks GA, 27 weeks CA. Prematurity related to cesarean section performed for IUGR. Brain ultrasound: intraventricular hemorrhage of III–IV degree. Discontinuous background activity. **High amplitude, biphasic delta waves more evident on the left temporal region**. Interburst interval with bilateral, positive, very slow waves. Absent delta brushes and theta temporal sequences. Follow-up: at 14 months hyperactivity and mild neurocognitive impairment

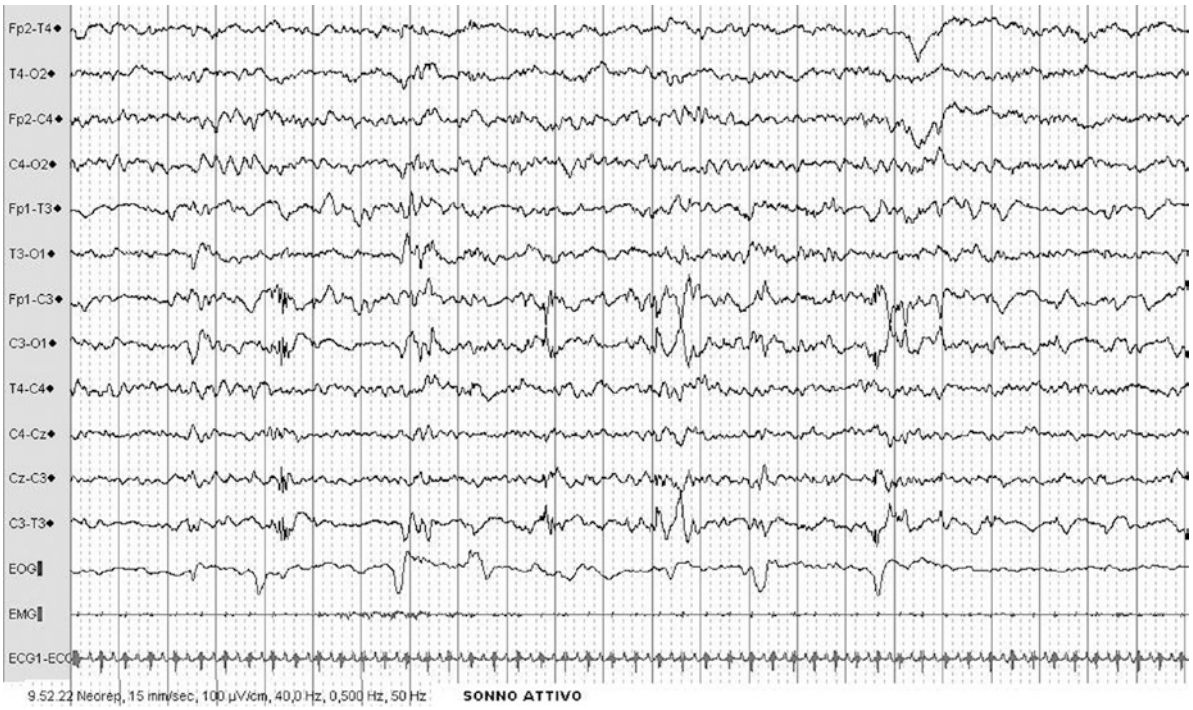

Fig. 22.42 See Fig. 22.43 caption

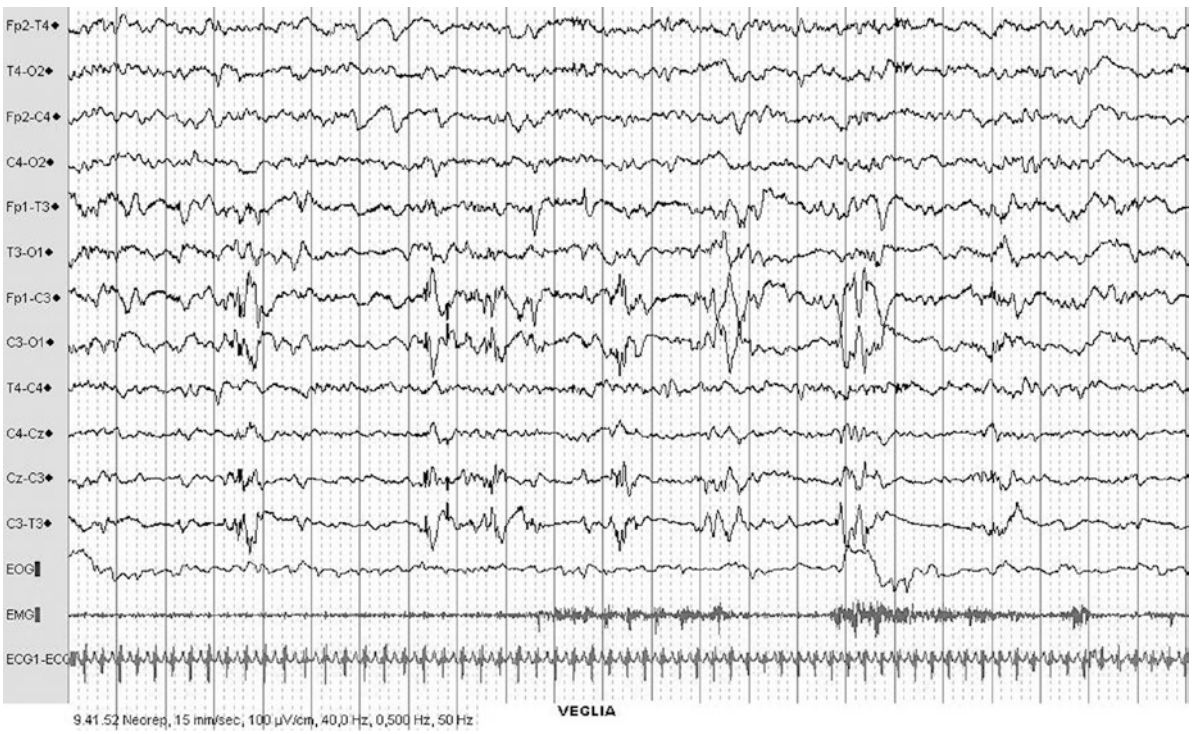

Fig. 22.43 36 weeks GA, 43 weeks CA. Uneventful pregnancy and delivery, the mother is a factor V Leiden mutation carrier. At birth asymmetric spontaneous movements (reduced in right side). Background activity is normal in the right side during wakefulness. Pattern characterized by **constant interhemispheric voltage asymmetry of background activity in the left hemisphere; slow theta-delta activity with superimposed spikes and polyspikes up to 200 mcV**. These EEG characteristics are observed both during wakefulness (Fig. 22.43) and during active sleep (Fig. 22.42). Brain MRI: hyschemic arterial infarction in the left median cerebral artery territory—factor V Leiden mutation heterozygosity. Follow-up: right-side pyramidal hemisyndrome, mild neurocognitive impairment (18 months old)

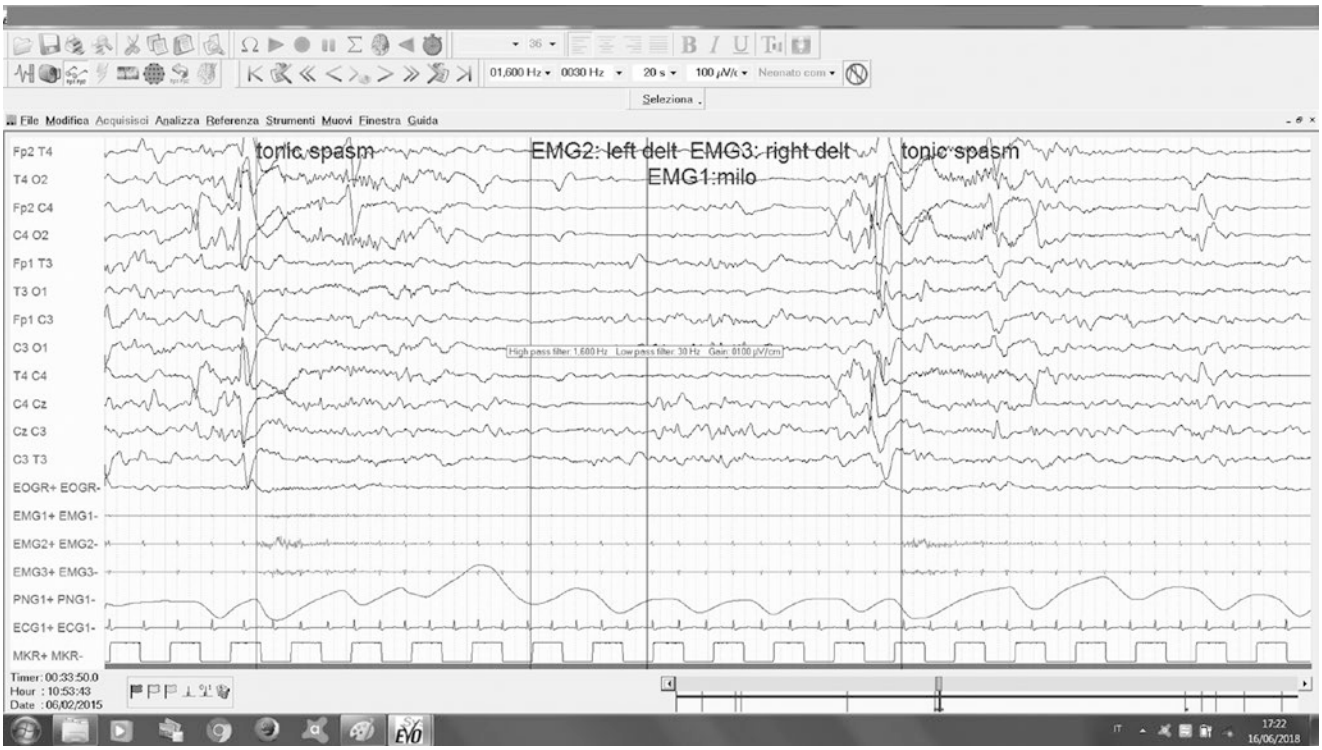

Fig. 22.44 40.6 weeks GA, 43.5 weeks CA. Uneventful pregnancy, till the last week, when the mother referred jerky repetitive fetal movements; urgent cesarean section due to oligohydramnios. Neonatal left arm and leg clonic seizures from the 1st day of life. **Neonatal focal symptomatic epilepsy**. Series of spasms in the second and third week of life. In therapy with PB 4 mg/kg/die, PHT 19 mg/kg/die. **Asymmetrical suppression-burst EEG pattern with high-voltage slow spike followed by high-voltage slow wave more evident in the right hemisphere, associated with a tonic spasm evident in the EMG channel. After the tonic spasm, a short run of alpha slow-voltage activity is evident in the right posterior region**. Two electro-clinical events are shown. Brain MRI: **right hemisphere polymicrogyria**

Box 22.3: Abnormal EEG Pattern/Transients

Positive rolandic sharp waves (PRSWs): they can be identified in the rolandic regions (phase reversal in C3 and C4): they are physiological if isolated, with onset between 28 and 32 weeks of CA, bilateral and asynchronous, with an amplitude lower than 150 mcV; if frequent, repetitive, unilateral, and of high amplitude, they can be expression of a focal hemorrhage or white matter injury (Fig. 22.45).

Positive temporal sharp waves (PTSWs): temporal sharp waves that according to morphology, polarity and frequency can represent underlying focal brain injury (Figs. 22.46, 22.47, and 22.48).

Spikes or sharp waves (frontal, temporal, central, occipital): recurrent spikes or sharp waves in the frontal, temporal, central, or occipital regions. They are usually single, bilateral, synchronous, and asynchronous between homologous regions of the two hemispheres (Figs. 22.45 and 22.47).

Multifocal slow sharp waves: multiple foci of high-amplitude slow waves, abundant and recurrent with an irregular rhythmicity. They can be associated with underlying diffuse brain injury (Fig. 22.49).

Focal rhythmic activity (at the vertex and/or in variable regions): the presence of rhythmic activity in beta, alpha, theta, or delta frequency, in short runs, superimposed to a normal background activity, is an unusual pattern in healthy newborns (Figs. 22.50 and 22.51).

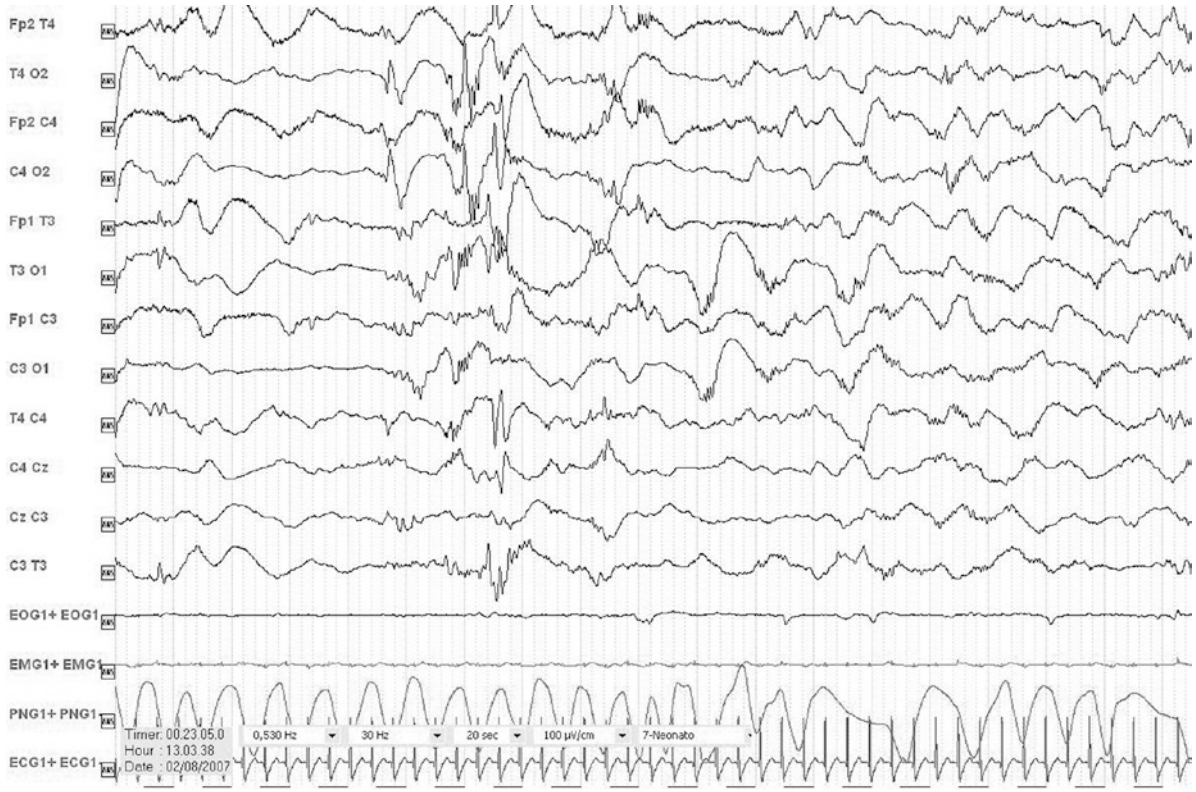

Fig. 22.45 31.2 weeks GA, 32 weeks CA. Uneventful pregnancy; at 31 weeks GA, fetal growth arrest with abnormal blood flows; the baby born through a cesarean section in **fetal distress with IUGR** (1280 g). Intubated and ventilated with surfactant replacement. Brain ultrasound: high echogenicity within right temporoparietal regions. Brain MRI: right hemisphere intraparenchymal hemorrhagic injury. During active sleep normal activity in the left hemisphere. In the right side, in occipital and central regions, spike, slow spike, and polyspike activity is present, within a right background activity with short periods of posterior flattening. **Multifocal slow spike activity associated with constant background asymmetry**

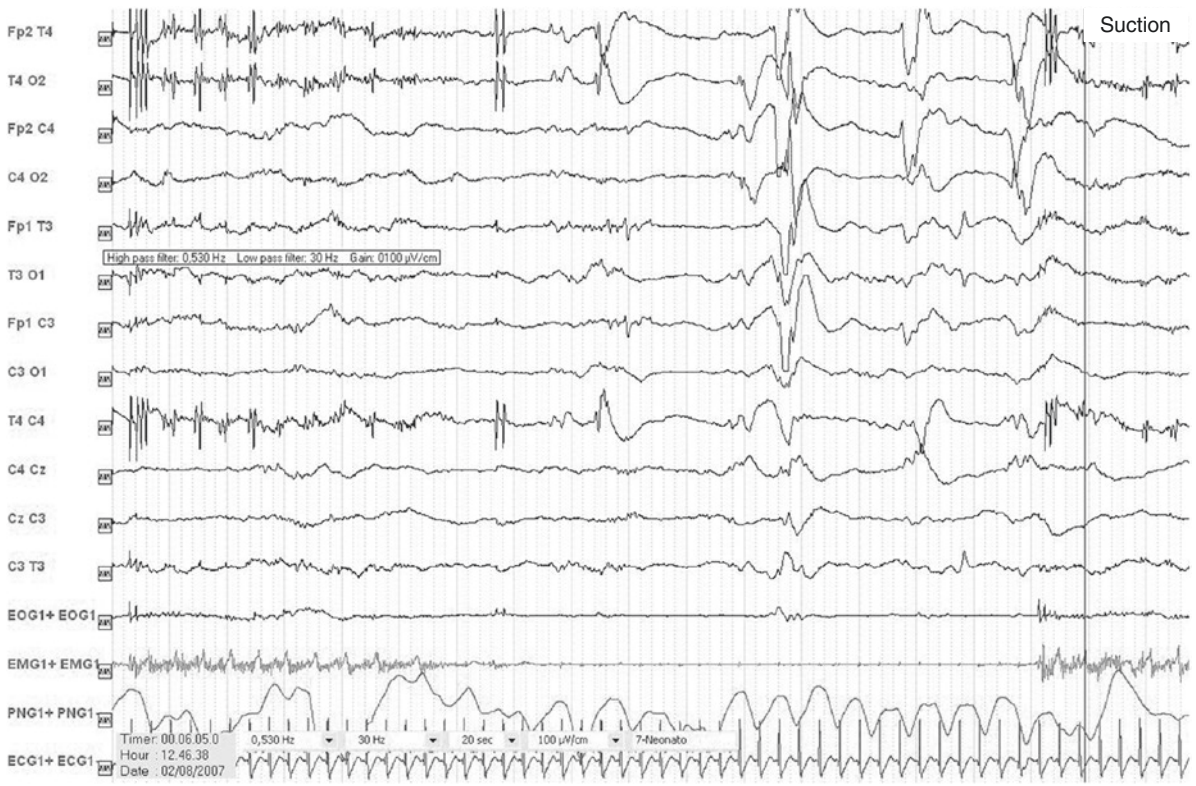

Fig. 22.46 Same newborn as in Fig. 22.45 Quite alert. Besides artifacts in T4, notice the positive slow- and low-voltage spike intermingled with a high-amplitude slow wave, followed by focal and isolated slow spikes in the frontotemporal region. **Positive temporal sharp waves (PTSWs)**

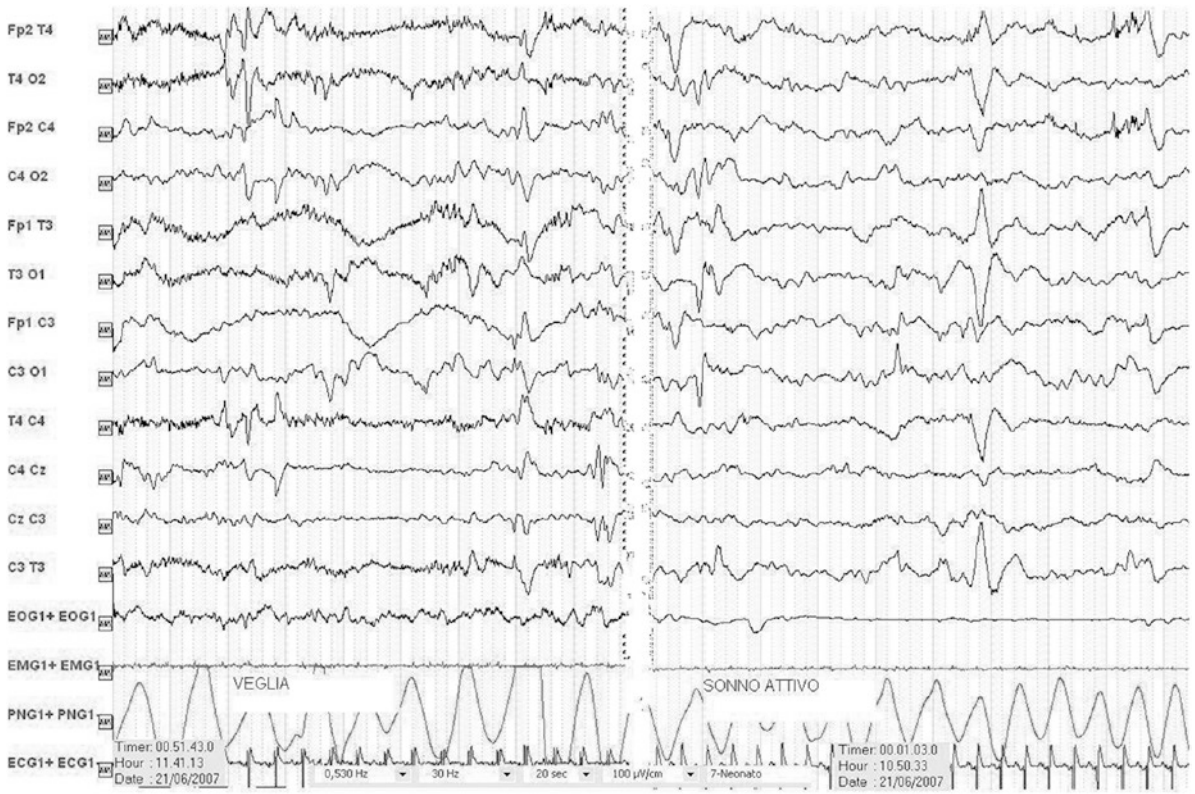

Fig. 22.47 36 weeks GA, 36.4 weeks CA. Urgent cesarean section due to fetal movements reduction in the last 48 h. At birth the newborn is hypotonic and hyporeactive. In the 1st day of life brisk, synchronous and asynchronous, erratic movements. **Prenatal hypoxic ischemic injury-hyperalert.** During wakefulness (in the left side of the image) normal background activity with superimposed right temporal slow wave and slow spikes high up to 250 mcV; during active sleep (right side) bilateral positive temporal slow spikes high up to 300 mcV are present. **Positive temporal sharp waves (PTSWs)**. Follow-up: normal development (8 months old)

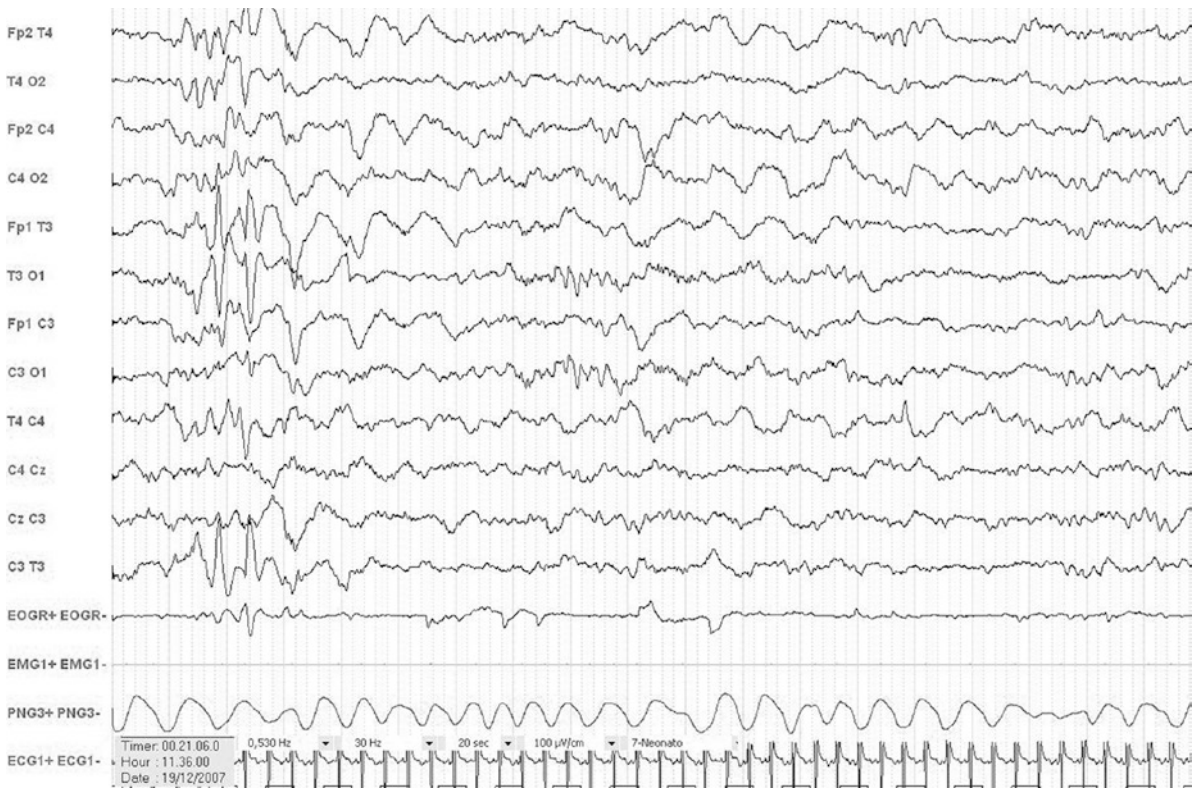

Fig. 22.48 38.4 weeks GA, 39.4 weeks CA. Fetal ascites. Normal delivery and perinatal period. 8 days of life, active sleep: **sequence of two-three phase-reversal high-voltage slow spikes in the left temporal region**. Background activity is normal for age. Brain MRI: megacisterna magna, **peritrigonal multiple micro-hemorrhagic lesions in the left hemisphere**. Follow-up: normal development (7 months old)

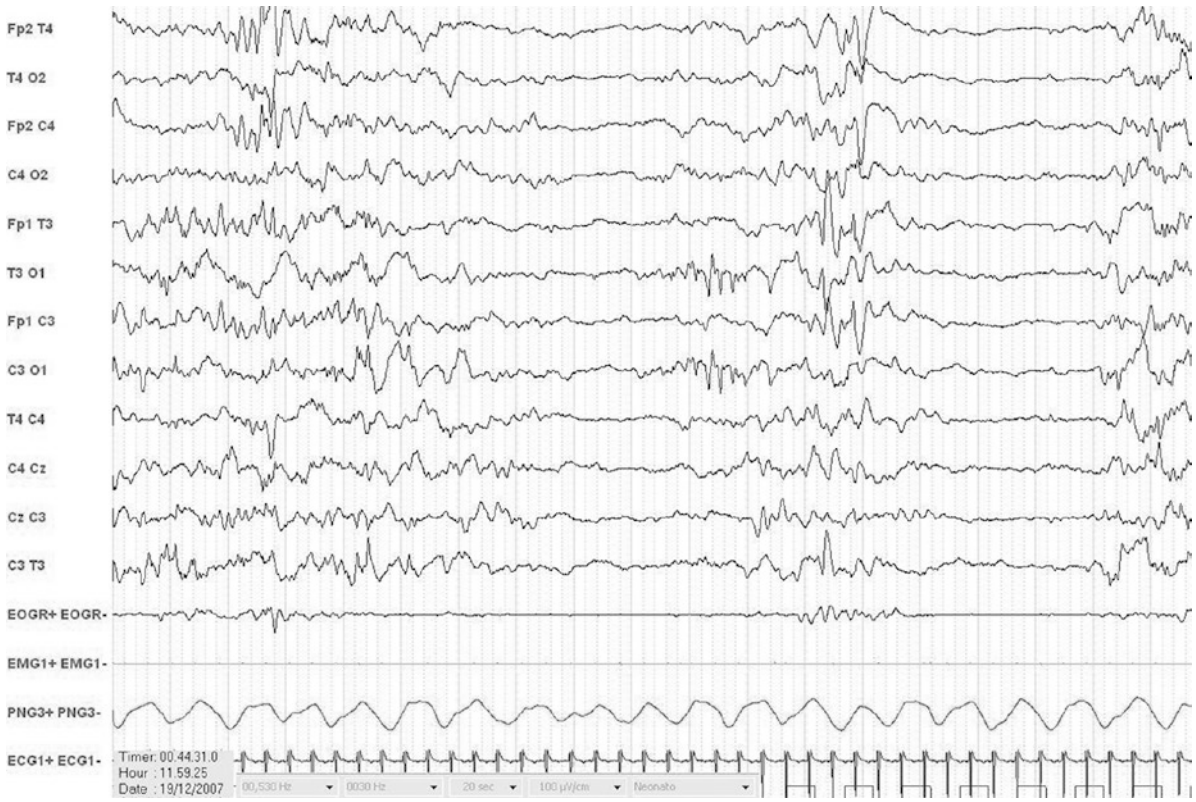

Fig. 22.49 Same newborn and same tracing as in Fig. 22.48. During quite sleep the tracè alternant pattern is quite discontinuous and asynchronous for the CA (**internal dyschronism**) with low-amplitude interburst interval. In addition **multifocal polymorphic slow spike** with voltage within 80–200 mcV, expressed independently in the left posterior frontal right and left regions

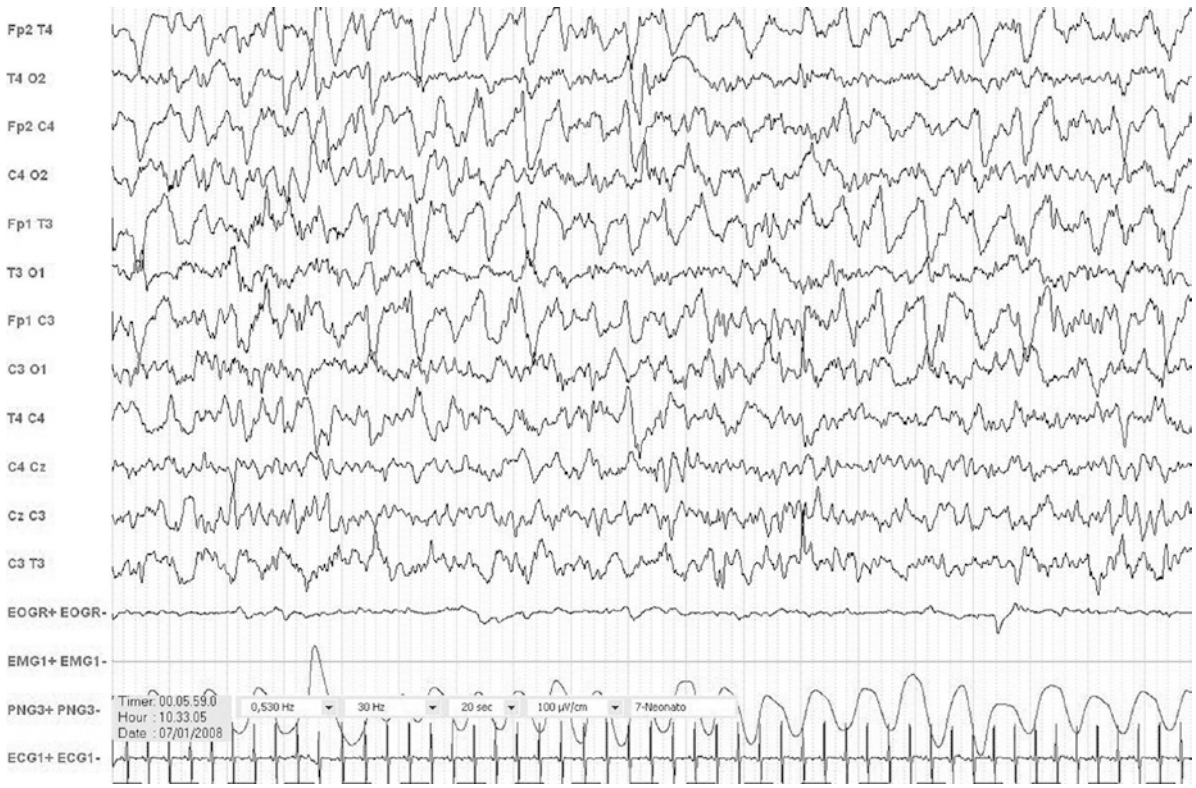

Fig. 22.50 34 weeks GA, 42 weeks CA. **Transient perinatal hypoxia due to respiratory distress in a premature newborn**. Irritability and benign hypnic myoclonus of newborn that started 3 days before the recording. Normal background activity in sleep and wakefulness. Notice in the figure transitional sleep with isolated sequences of 1–2 Hz sharp and rhythmic activity limited to bilateral anterior regions, lasting 3–18 s. **Unusual focal anterior and rhythmic activity.** Follow-up: normal development (30 months old)

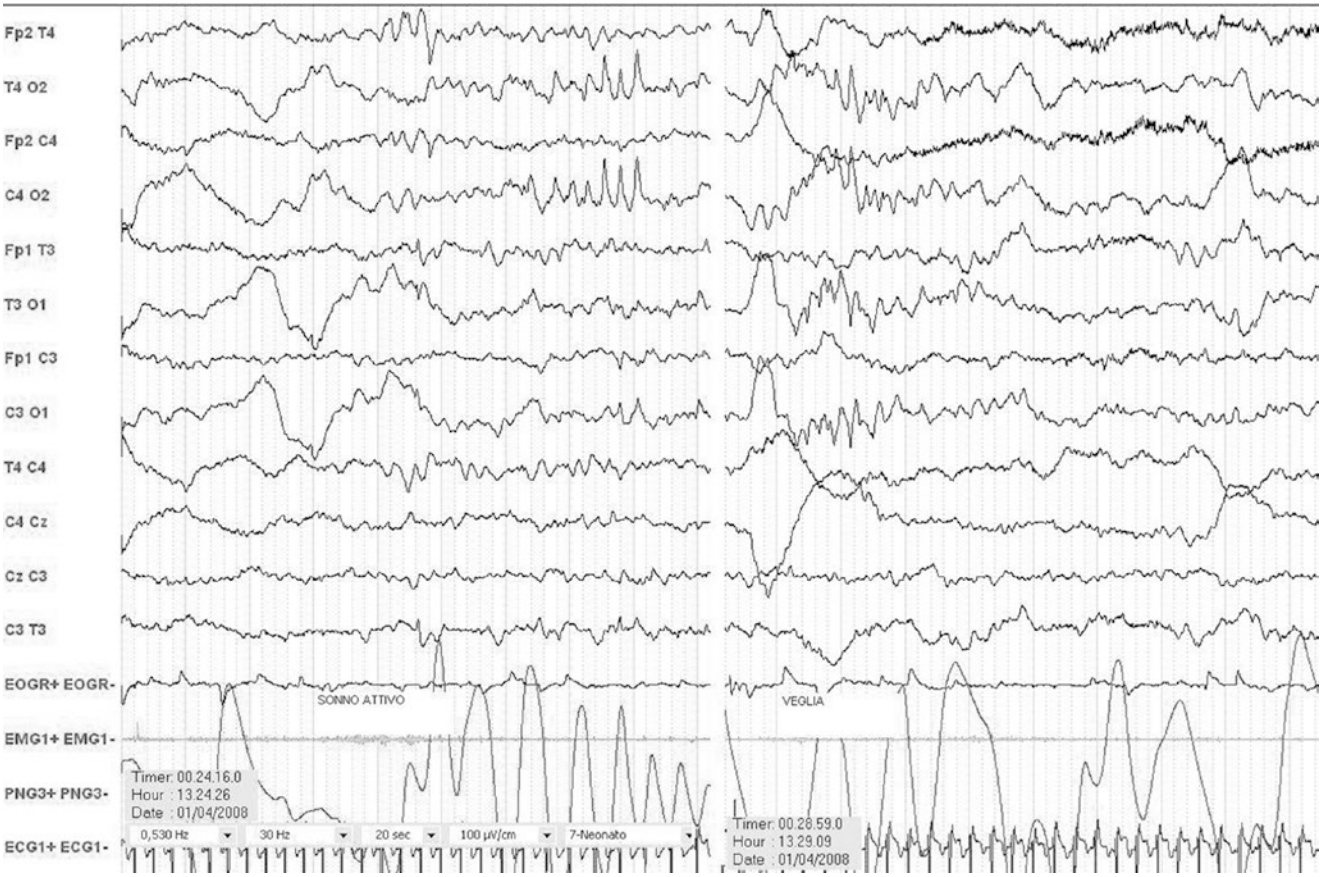

Fig. 22.51 GA 38 weeks, CA 41 weeks. Uneventful pregnancy and delivery. **Irritability at 3 weeks of life**. EEG recording include normal cycles of wake, tracé alternant in quiet sleep and active sleep. In active sleep in O2 (left side of the figure) and during awake state in O1 (right side of the picture), 2–4 s sequences of sharp theta and bilateral (asynchronous) activity with an amplitude up to 120 mcV. **Unusual focal and rhythmic posterior activity**. Follow-up: normal neurodevelopment at 6 months of age

Box 22.4: Ictal Epileptic Abnormalities

Focal or unifocal: sequence of high-amplitude sharp waves with a focal onset, with a range frequency between 5 and 10 Hz, monorhythmic, with sudden onset and end, usually related to clinical focal seizures (Figs. 22.38, 22.52, 22.53, 22.54, 22.55, 22.66, and 22.67).

Focal pseudo-beta-alpha-theta-delta: ictal EEG pattern characterized at the beginning by a low-amplitude rapid electrical activity faster than 12 Hz followed by a frequency reduction up to 4–7 Hz and then up to 0.5–3 Hz with a focal localization (Figs. 22.54, 22.55, and 22.56).

Multifocal activity associated with a pathological background: Multifocal ictal sequence with a synchronous or independent onset with either a fast or variable frequency (sometime with a slow rhythm). An abnormal background activity of low voltage is constantly associated during the inter-ictal periods and with a suppression-burst pattern in the most severe cases (Figs. 22.56, 22.57, 22.58, 22.59, 22.60, 22.61, 22.62, 22.63, and 22.64).

Ictal activities of low frequency associated with a low-voltage background EEG activity: they are characterized by sharp waves at 1 Hz with either focal or multifocal and independent localizations (Figs. 22.58, 22.59, and 22.65).

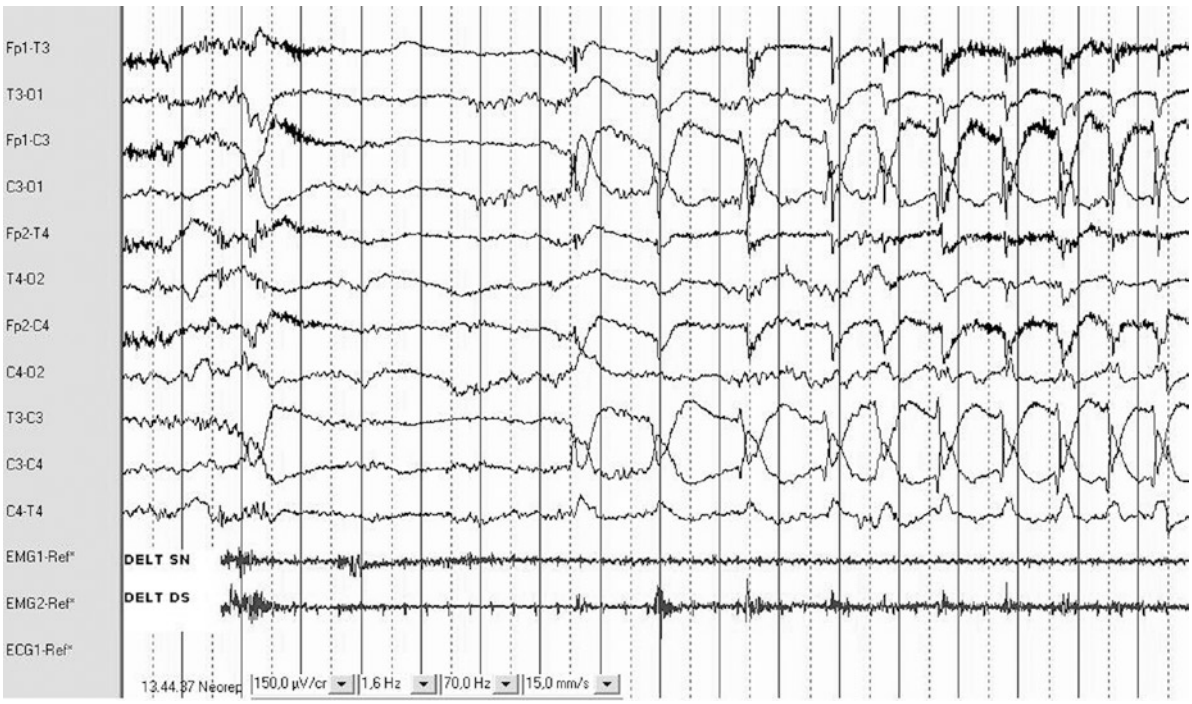

Fig. 22.52 See Fig. 22.53 caption

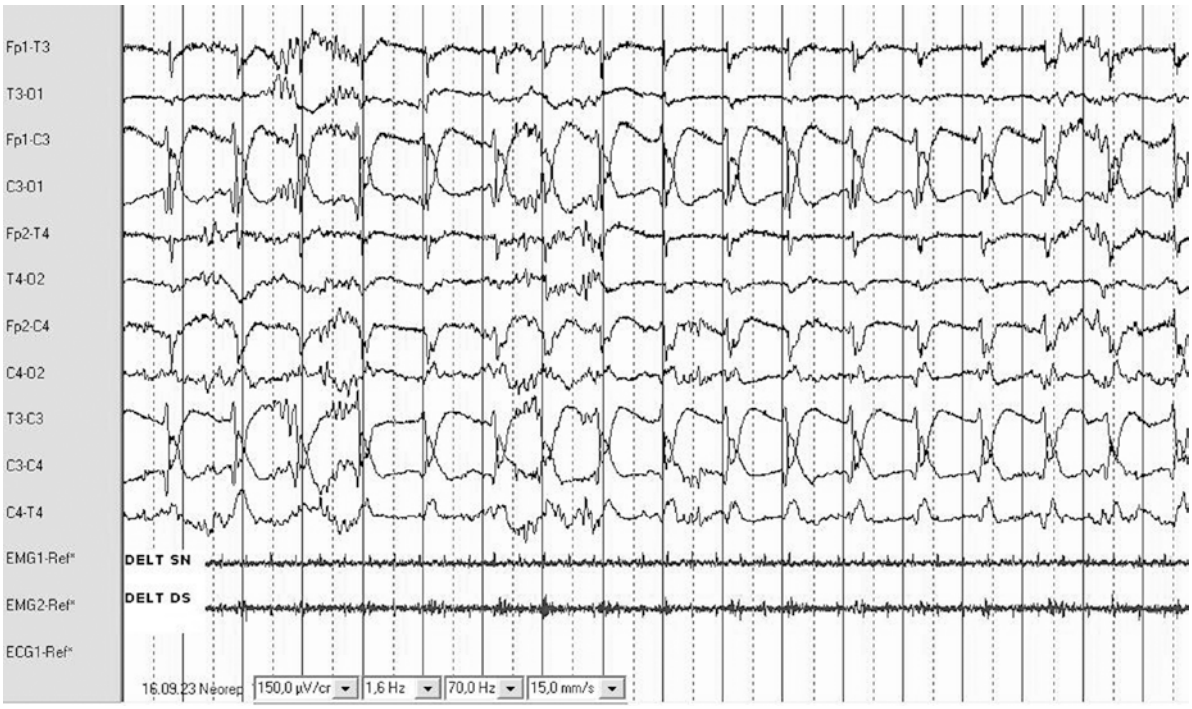

Fig. 22.53 35 weeks GA, 35 weeks CA: Tuberous sclerosis suspected during prenatal ultrasound due to the presence of cardiac rhabdomyomas. At birth the newborn is hypotonic and hyporeactive. Brain ultrasound investigation: multiple periventricular echodensities. On the 3rd day of life, recurrent short (lesser than 1 min) focal proximal right arm clonic seizures associated with staring. **Unifocal (left fronto central) ictal EEG pattern** (the first consecutive 40 s of a seizure are shown in Figs. 22.52 and 22.53): after 5 s EEG flattening associated with a brief bilateral arms contraction seizure discharge arise from the left posterior areas with alpha-like activity lasting less than 2 s, followed by repetitive rhythmic (1/s) spike and high-voltage (up to 180 mcV) slow wave complexes in the fronto-central region. EMG polygraphy of the right deltoid channel shows the rhythmic proximal jerks strictly associated with the spike-slow wave complexes. The seizures (aware, clonic focal motor) end spontaneously in 1–3 min. During the EEG recording (110 min), 14 similar electro-clinical seizures were recorded. Brain MRI: several cortical tubers (the most evident in the left rolandic region). **Focal neonatal symptomatic (tuberous sclerosis complex) epilepsy**. Follow-up: West syndrome at fourth months followed by Lennox Gastaut syndrome with severe neurocognitive impairment (24 months of age)

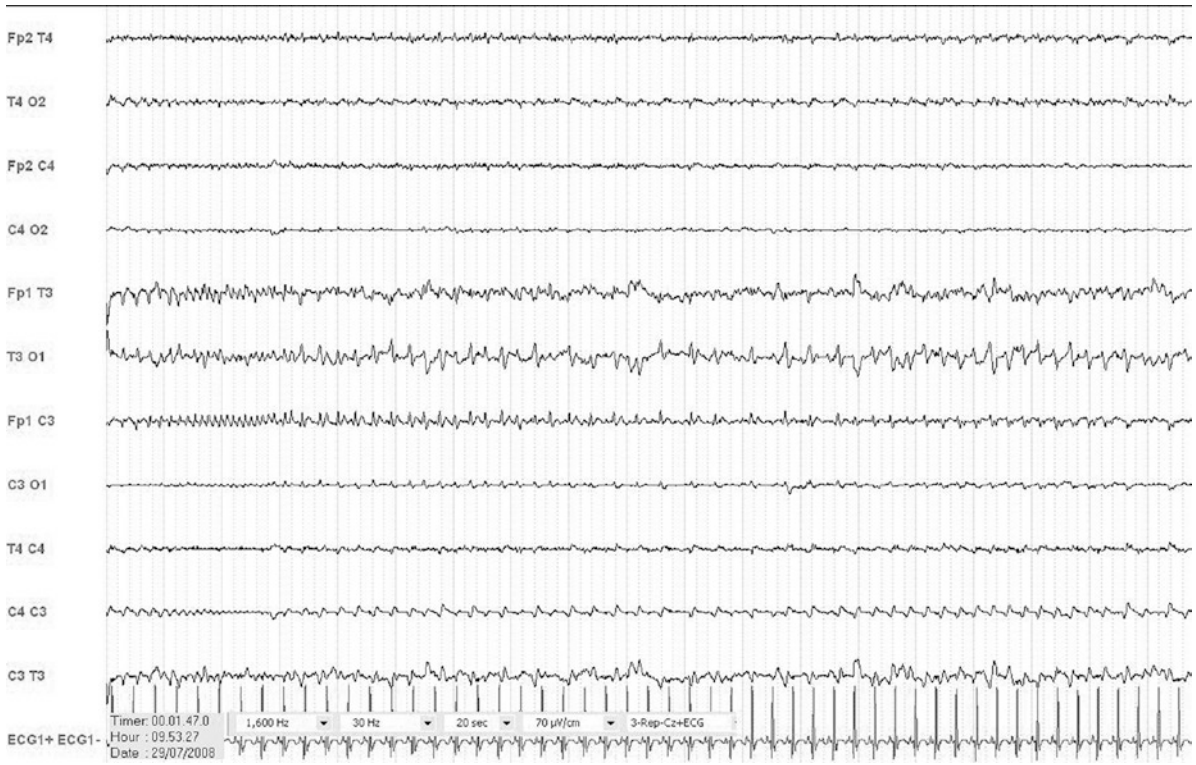

Fig. 22.54 See Fig. 22.55 caption

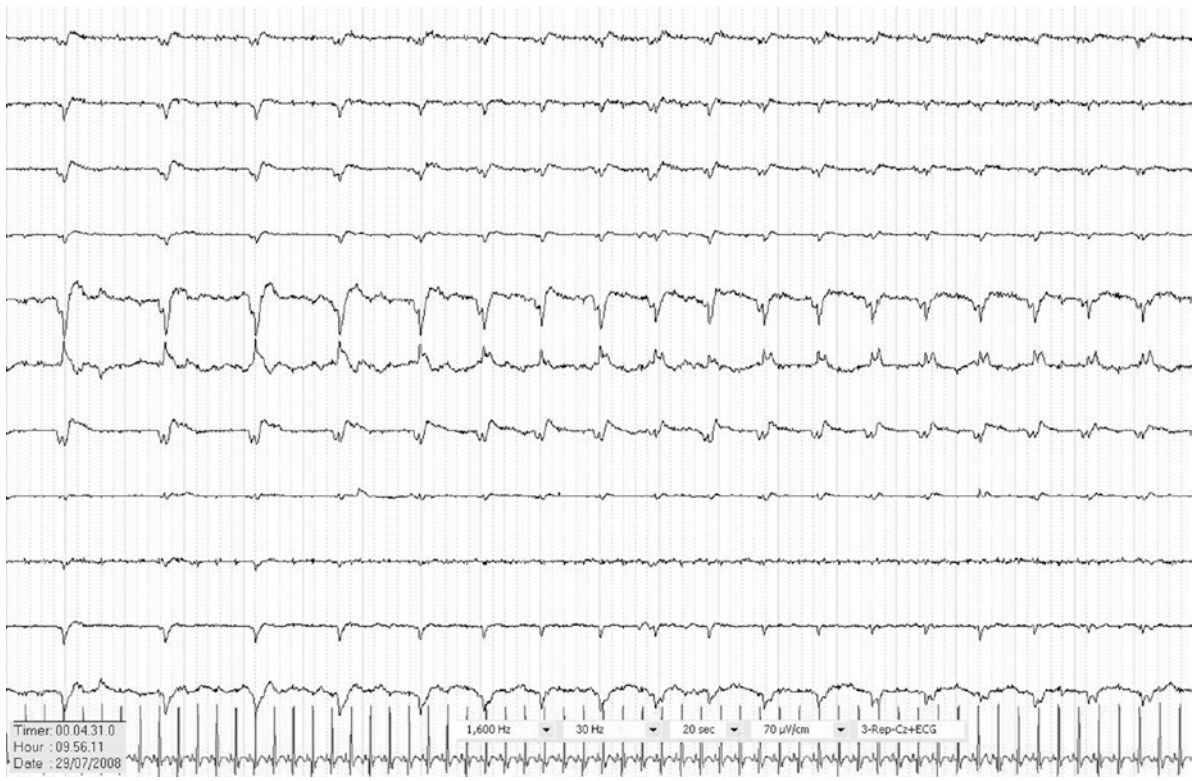

Fig. 22.55 35 weeks GA, 35.3 weeks CA. Pregnancy complicated by maternal-fetal Rh-isoimmunization. Uneventful delivery. Birth weight 2750 g, Apgar score 8–9. After 7 min deteriorating of general condition: pH 6.9, BE-19 mmol/L, CO_2 43 mmHg, lactic acid 24 mmol/L, glycemia 37 mg/dL, Hb 4.5 g/dL. At 3 days of life, the newborn became hypotonic and hyporeactive. The EEG background activity is constantly lower than 30 mcV, and **repetitive infraclinical seizure discharges characterized by left alpha > beta and sharpened theta activity** (Fig. 22.54) **evolving to rhythmic slow spikes and slow wave complexes** higher in the right hemisphere. The discharge seems to spread to the right hemisphere; however it is more likely an electrical signal diffusion. **Low voltage undifferentiated tracing**. **Cerebral cortical-subcortical anoxia due to isoimmunization.** Brain MRI (4 days): cortical and subcortical malacic lesions involving gray and with matter basal ganglia and midbrain nuclei. Follow-up: severe dystonic–hypotonic quadriparesis associated with static encephalopathy with abnormal social interaction. (24 months old)

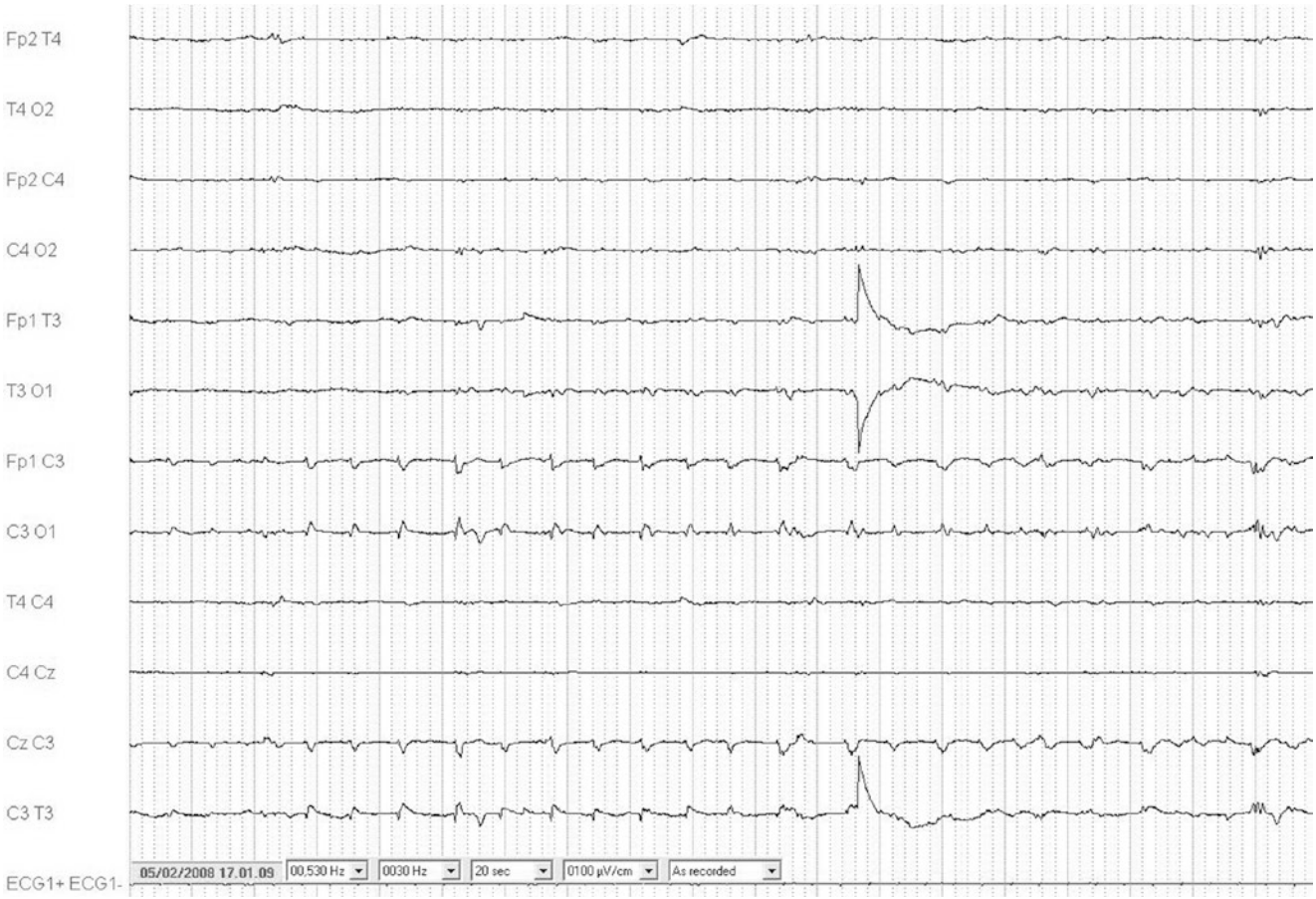

Fig. 22.56 40 weeks GA, 43.3 weeks CA. Uneventful pregnancy and delivery. At 22 days of life ***Streptococcus beta-haemolyticus*** **type B encephalitis associated with convulsive > electrical status epilepticus. Induced thiopental sodium coma with infraclinical multifocal recurrent seizures with electro-clinical dissociation and severely abnormal background activity**. Follow-up: severe neurocognitive impairment >West syndrome at 6 months >developmental encephalopathy with AED's resistant epilepsy >died at 3 years old. 1 h after thiopental sodium therapy reduction to 2.5 mg/kg/h, electrical focal (C3) seizure activity recurs, characterized by rhythmic (1/s) low-amplitude (lesser than 40 mcV) slow spikes

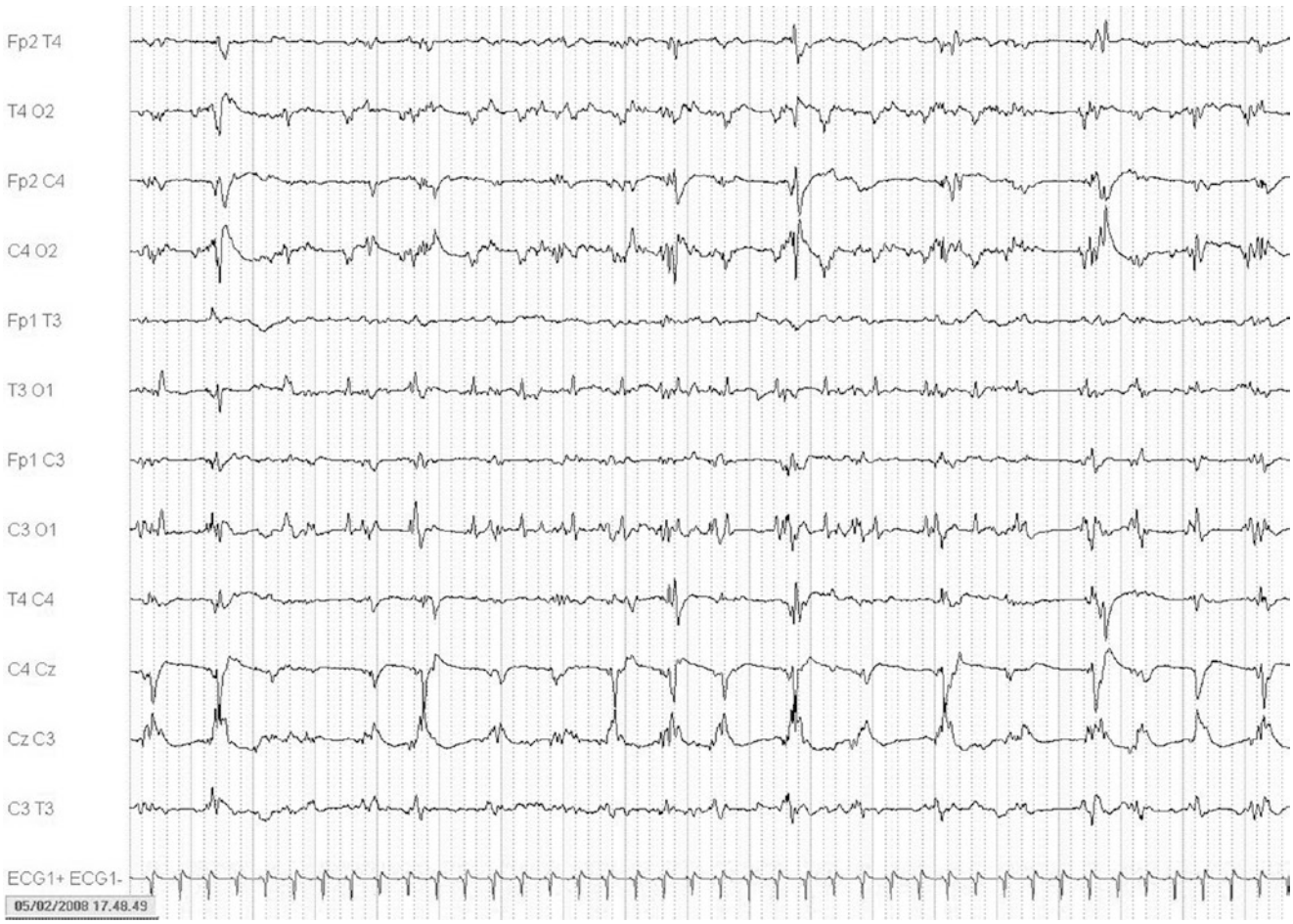

Fig. 22.57 40 weeks GA, 43.3 weeks CA. Uneventful pregnancy and delivery. At 22 days of life ***Streptococcus beta-haemolyticus*** **type B encephalitis associated with convulsive > electrical status epilepticus. Induced thiopental sodium coma with infraclinical multifocal recurrent seizures with electro-clinical dissociation and severely abnormal background activity**. Follow-up: severe neurocognitive impairment >West syndrome at 6 months >developmental encephalopathy with AED's resistant epilepsy >died at 3 years old. Eighteen minutes later, **bilateral independent electrical seizures** arise from occipital, left and right, and central region with different morphology: rhythmic slow spikes (left occipital), rhythmic polyspike complexes (right occipital), rhythmic slow spike, and slow wave complexes high as 130 mcV

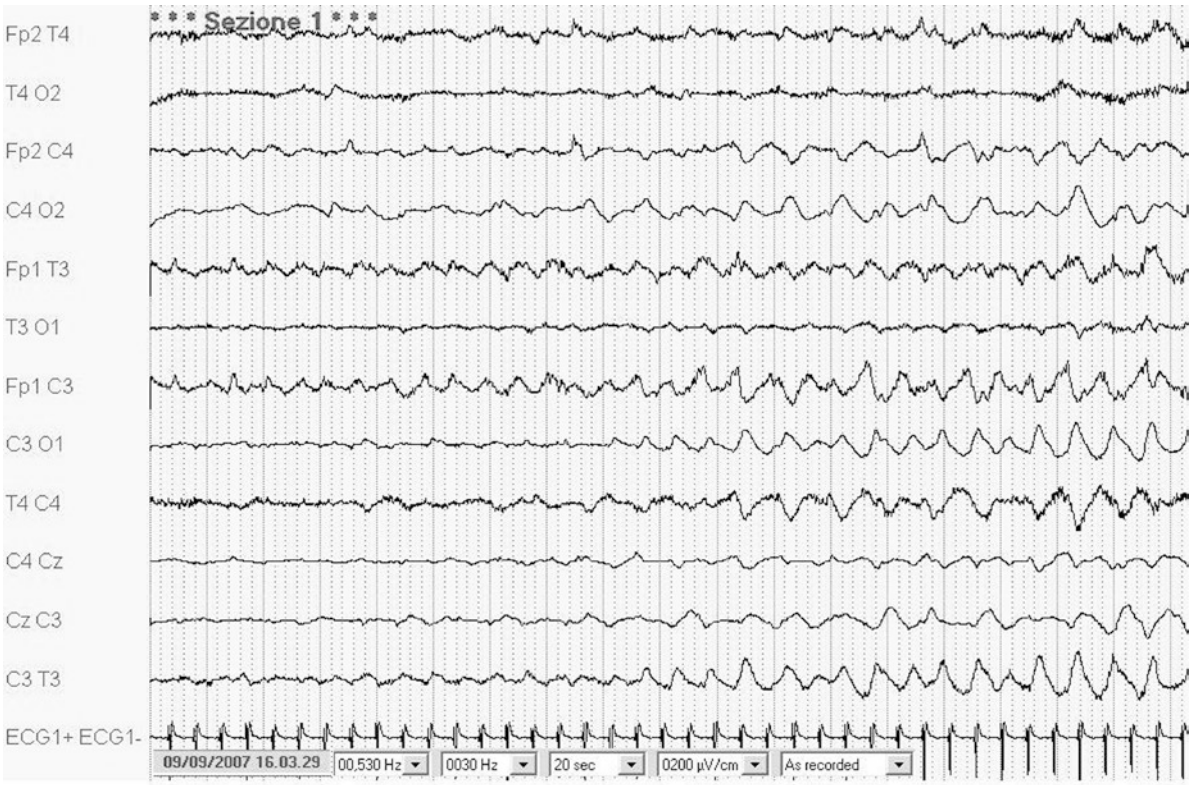

Fig. 22.58 See Fig. 22.59 caption

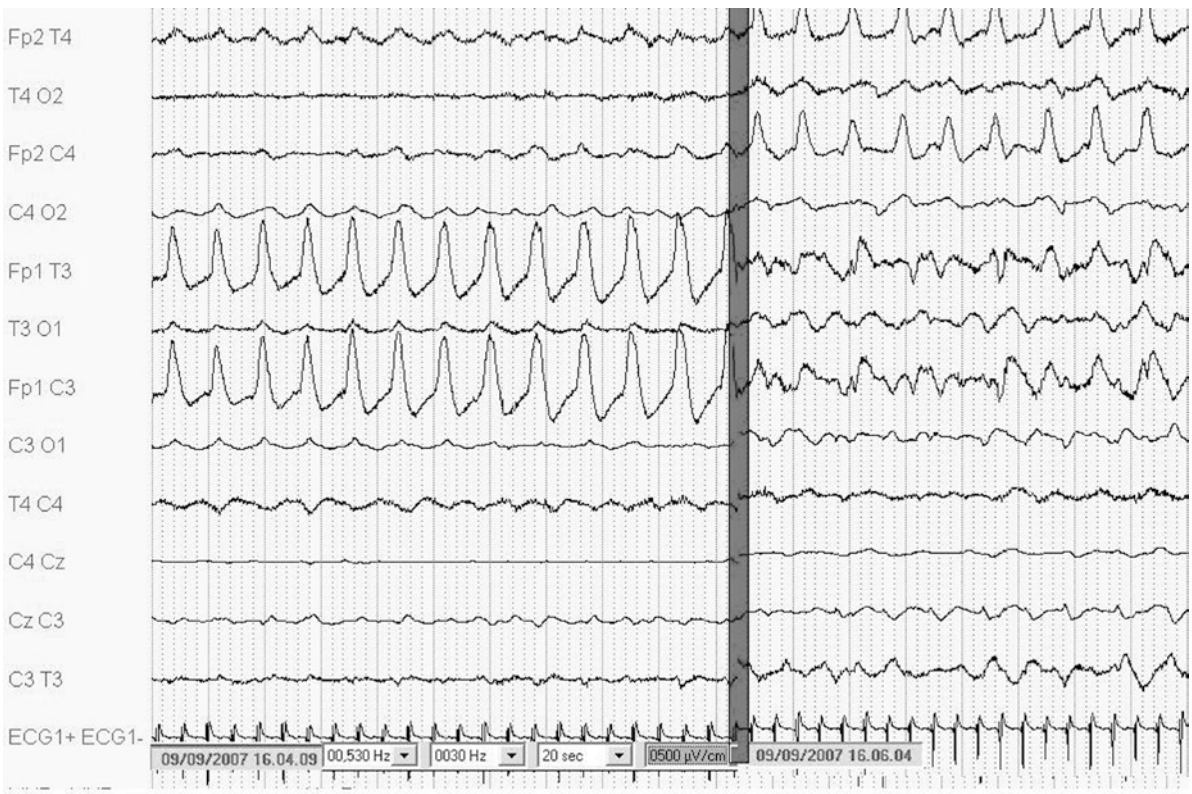

Fig. 22.59 Same newborn as in Fig. 22.30 40 h after, mechanical ventilation, and hypothermia treatment: **Acute transitory hypoxic ischemic encephalopathy**. Within a constantly low-voltage tracing (amplitude between 5 and 30 mcV), in Fig. 22.58 infraclinical ictal sharpened delta activity high up to 300 mcV in the fronto-central left region, with diffusion to the adjacent region. After 40 s, in Fig. 22.59 (in the left side of the image), a seizure infraclinical discharge characterized by sharpened delta activity high up to 600 mcV is present in the frontal region. Two minutes after (right side of the image) the seizure abates in the left region, becoming focal in the right anterior region. **Multifocal and low-voltage/slow-frequency discharges superimposed on a low-voltage background activity**

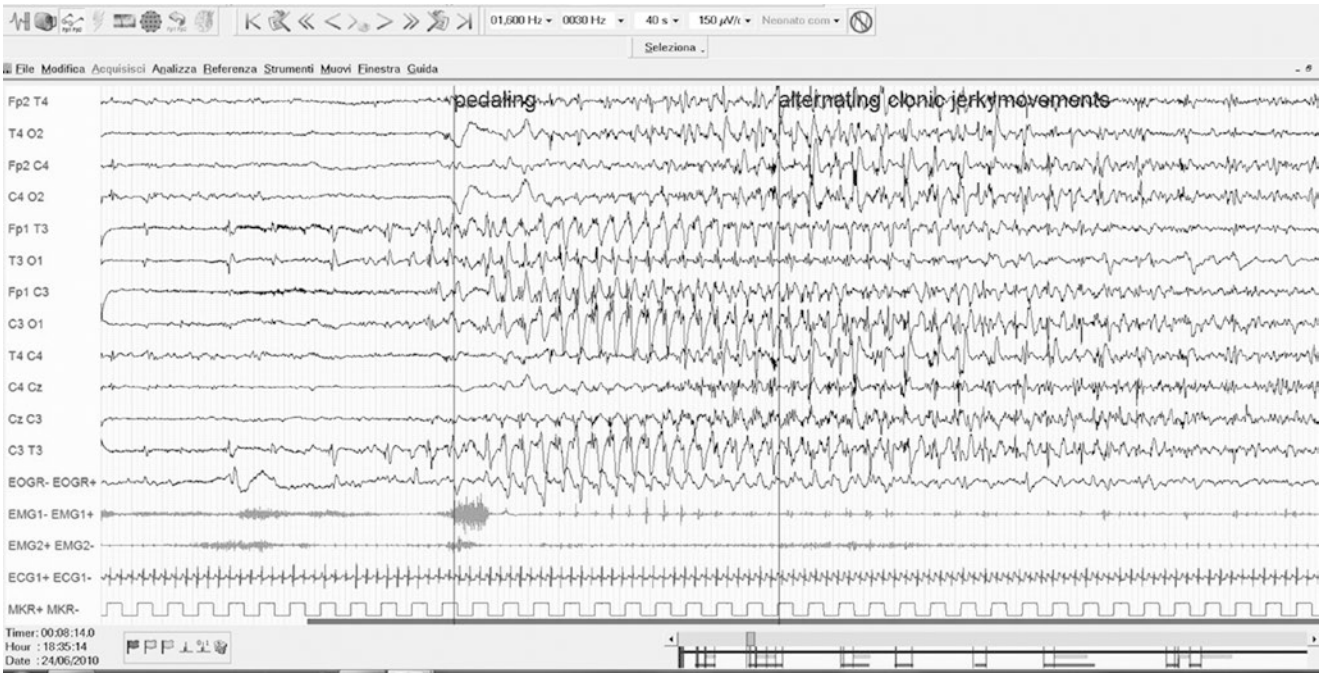

Fig. 22.60 39 weeks GA, 42.3 weeks CA. Pregnancy complicated by fetal growth retardation; cesarean section due to breech presentation, 2540 g (SGA), APGAR: 4-7-10. Relative macrocephaly. At birth the newborn is hypotonic and hyporeactive. Transient hypoglycemia in the first 2 days of life. From the 3rd day of life repetitive AED's resistant polymorphic seizures (clonic bilateral asynchronous, oral automatisms, spasms, and pedaling of the legs). The newborn is comatose. The background activity is depressed. **Two independent seizures arise from the left and then on the right hemisphere evolving with polyspikes-wave rhythmic complexes associated with pedaling of the legs and clonic jerks of the right and then left deltoid (see EMG polygraphy)**. The focal bilateral seizures end in 1 min followed by a flat trace (not shown). *Time base 7.5 mm/s*

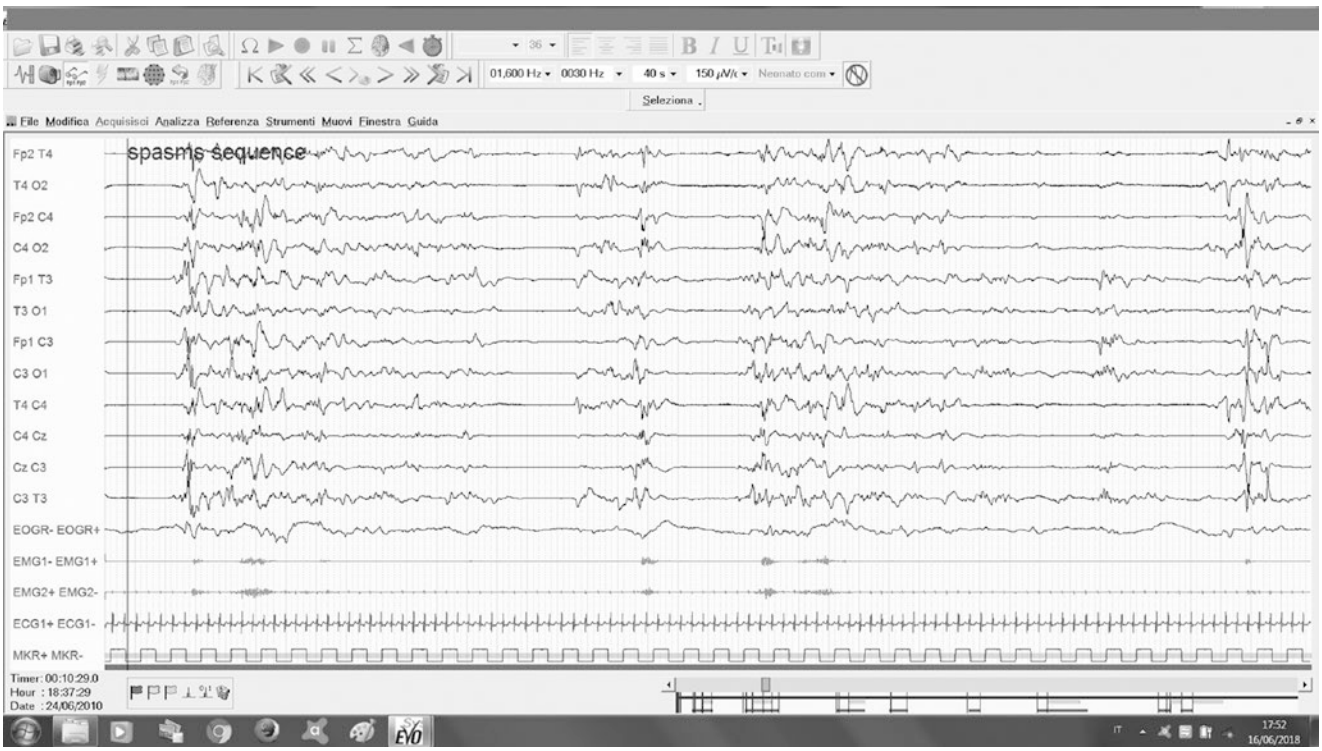

Fig. 22.61 Same newborn and same recording of Fig. 22.60). **A sequence of spasms** occurs 40 s after the end of the seizure shown in this figure. The spasms, clearly documented by EMG polygraphy, are symmetrical, associated with a bilateral high-voltage polyspikes slow wave complex and recur within an ictal suppression-burst pattern, with flat periods lasting 4–8 s. PHT high-dosage i.v. therapy, with blood levels above 20 mcg/mL, controlled the seizures with disappearance of the suppression-burst pattern. Brain MRI and extended metabolic blood and cerebrospinal fluid analysis were normal. Genes panel analysis for early onset epileptic encephalopathy (EOEE) detected a **SCN2A causative de novo mutation**. **Neonatal genetic epilepsy within a condition of Early Onset Epileptic Encephalopathy (EOEE)**. *Time base 7.5 mm/s*

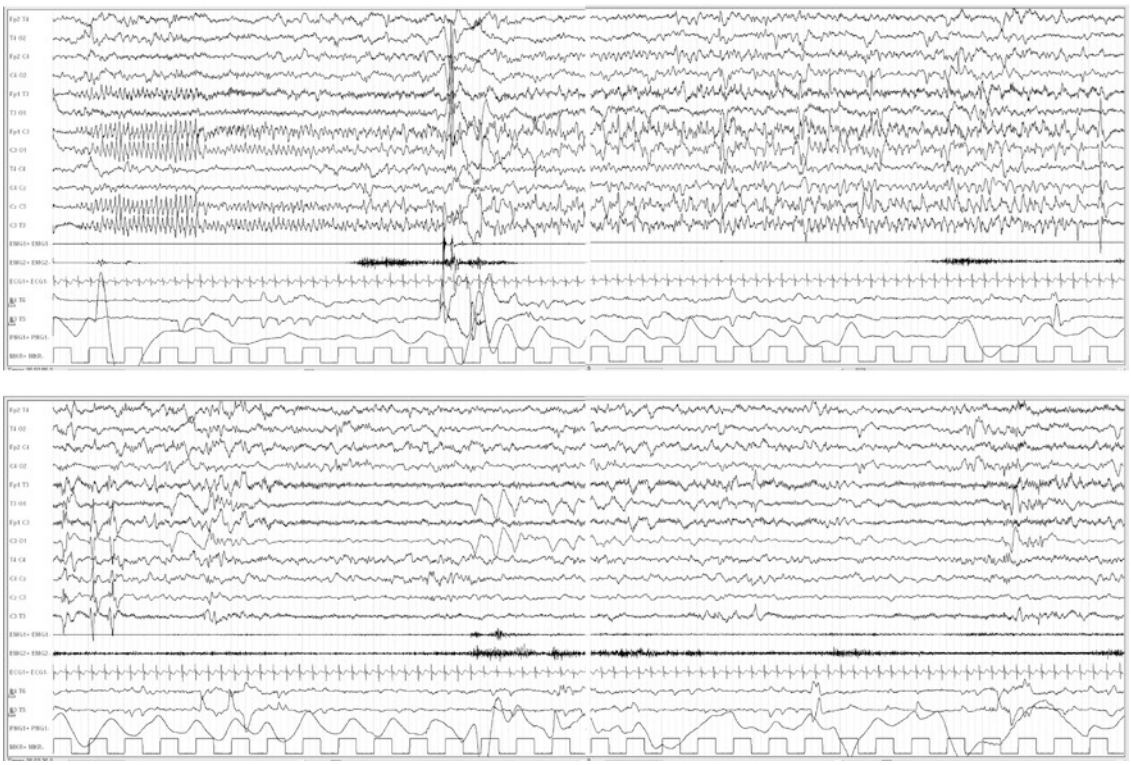

Fig. 22.62 39 weeks GA, 39.2 weeks CA. Uneventful pregnancy and delivery. Outborn. Referred apneic seizures in the first 2 days of life, then transferred in our hospital. In the figures **electro-clinical seizures** arose either **from the left** (or the right) central regions with slow >high voltage, fast, rhythmic sharp waves activity. Then abruptly evolved to rhythmic slower activity with sharply contoured theta activity intermixed with spikes. Post-ictal background activity is asymmetrical and excessively discontinuous for CA. The electrical seizure **tends to spread to the contralateral side**. The clinical component was characterized by oral automatism followed by asymmetrical tonic posturing, bradypnea, and tonic eye deviation. Brain MRI and extended metabolic blood and cerebrospinal fluid analysis were normal. Genes panel analysis for early onset epileptic encephalopathy (EOEE) detected a **KCNT1 causative de novo mutation, as the cause of a neonatal onset malignant migrating focal seizures syndrome**. *Time base 10 mm/s*

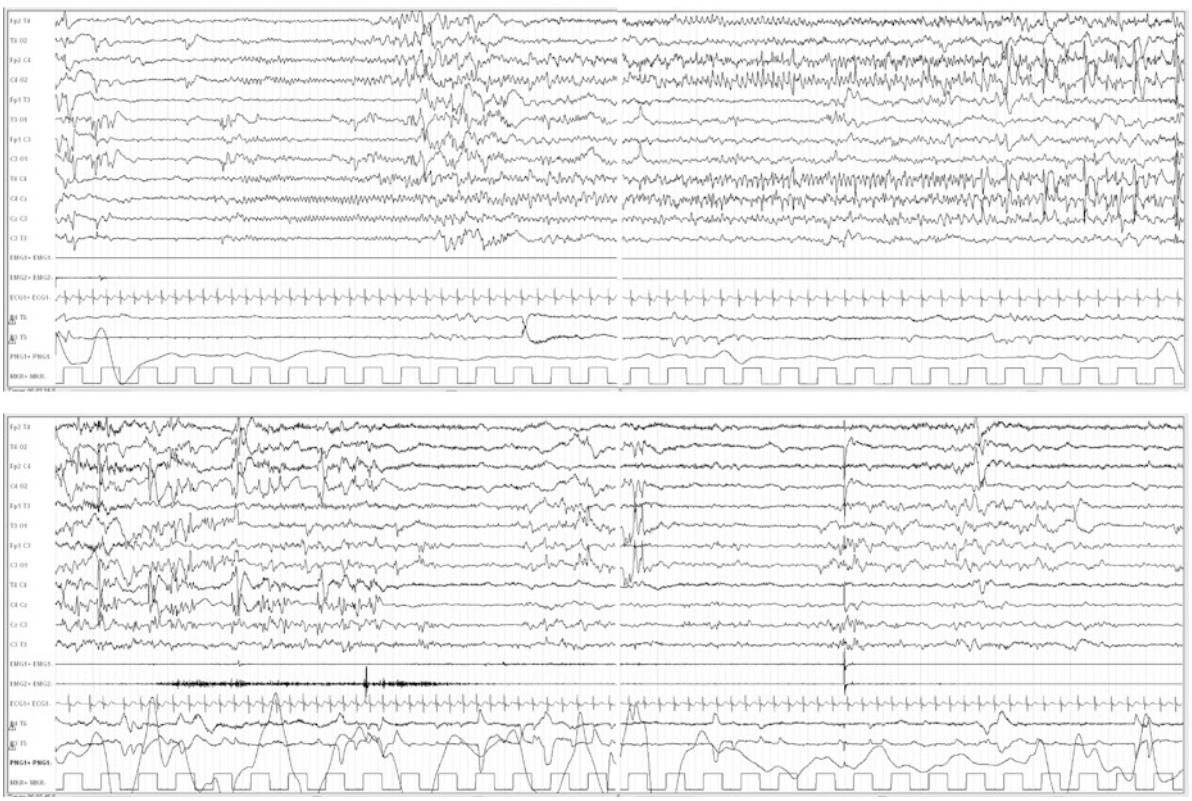

Fig. 22.63 Same newborn and same recording of Fig. 22.62. The same ictal pattern arose from the right hemisphere. *Time base 10 mm/s*

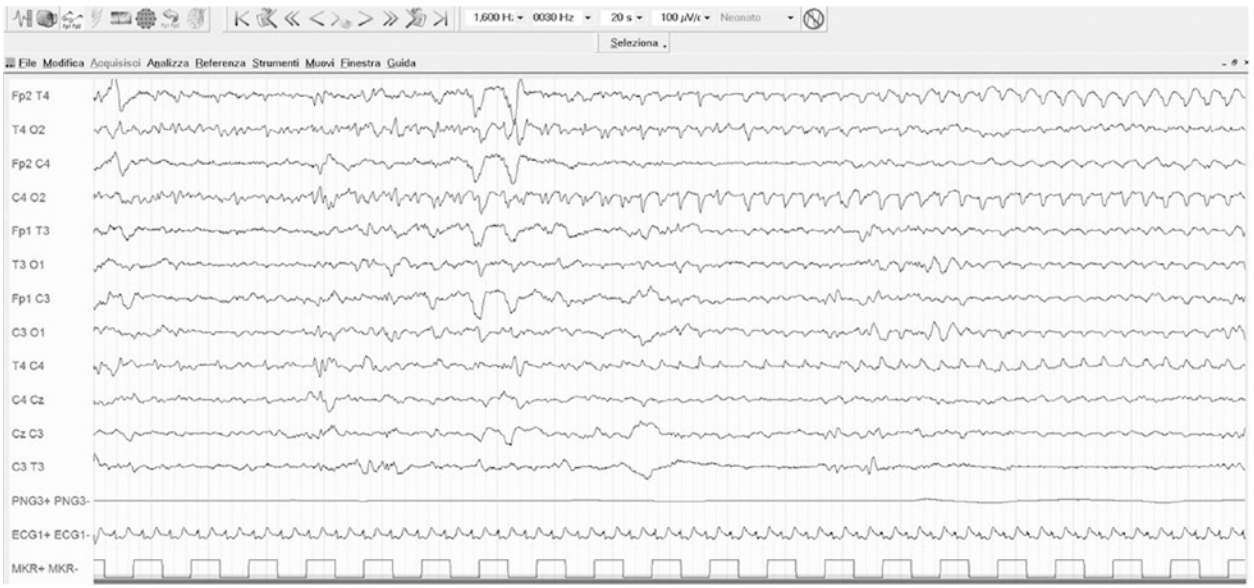

Fig. 22.64 38 weeks GA, 40 weeks CA. Normal pregnancy and delivery. In the 1st day of life, bilateral asynchronous focal clonic seizures and oral-buccal-lingual seizures occurred, controlled after PB and PHT iv therapy. The newborn, however, was lethargic and hyporeactive. **During a long-lasting EEG monitoring during all the night, 14 infraclinical electrical-only seizures (1–3 min) were detected**. In the figure a seizure discharge, characterized by rhythmic theta sharp activity evolves on the right hemisphere from the posterior to the temporal region and then to the centro-temporal region of the left hemisphere with a similar but asynchronous pattern between the two hemispheres. Brain MRI and extended metabolic blood and cerebrospinal fluid analysis were normal. The pattern is suggestive for a neonatal symptomatic epilepsy, presumed genetic in nature, as **malignant migrating focal seizures**

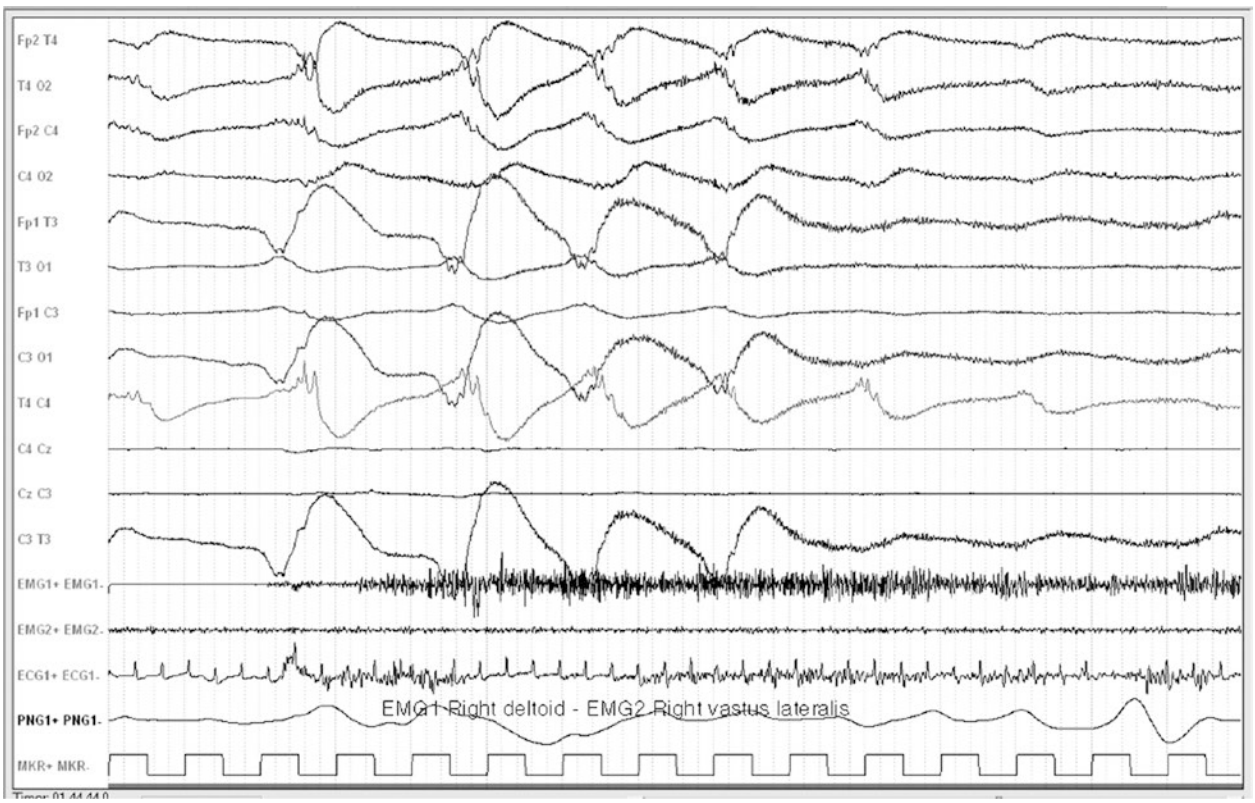

Fig. 22.65 28 weeks GA, 28.3 weeks CA. Prematurity: after a normal pregnancy, urgent cesarean section for maternal reasons. The newborn was unreactive and lethargic. **Prolonged infraclinical sequences of bilateral, synchronous, very slow, high-amplitude delta waves, more pronounced in the temporal areas**, which are smooth and are associated with slow-voltage rhythmic sharpened theta activity. The sequences described might be epileptic in nature. Follow-up: normal brain ultrasound, normal psychomotor development (16 months)

22.7 Iconography of the Abnormal EEG

The following information in the caption of each single image report: the acronym P stands for pathological trace, GA for gestational age, expressed in weeks, and CA for the conceptional age, expressed in weeks. In summary a short comment of the pathology is also provided to define the clinical condition for which the examination has been performed.

Regarding the iconography shown, in Figs. 22.21, 22.22, 22.27, 22.39–22.41, and 22.65 peculiar pathological findings of the premature tracing are reported. In Figs. 22.19, 22.20, 22.30–22.37 inactive and suppression-burst patterns have a completely different clinical evolution, to testify how these patterns, associated generally with unfavorable prognosis, could have a different evolution in relation to different clinical conditions. In Figs. 22.42–22.44, 22.52, 22.53, 22.66, and 22.67, the constantly asymmetric pattern, relative to both the underlying activity and the critical abnormalities, is related to a structural, congenital, or acquired focal etiology. In Figs. 22.38, and 22.54–22.59, it is emphasized how the characteristics of the critical discharge can be modified according to the severe alteration of the underlying background activity. In Figs. 22.45–22.51, the abnormalities with spike and/or sharp wave morphology, focal or multifocal, require an extreme caution in interpretation, and they must be constantly correlated with the characteristics of the basic activity of the recording. Figures 22.23–22.27, with regard to discontinuity (with external and internal dyschronism) and to asynchrony, show that a careful evaluation of the clinical picture is necessary. The evolution of the electrical pattern must be also taken into account to provide an adequate, diagnostic and prognostic judgment. Similarly, Figs. 22.50 and 22.51 show rhythmic activities at a variable location for which caution is required with respect to an interpretation of "normal" or "abnormal" finding. In Figs. 22.28, 22.29, and 22.60–22.64 are reported peculiar features both of the background activity and ictal activity related to genetic conditions, documented or suspected.

All the children, whose iconography has been reported, have been evaluated personally by at least one of the authors.

Acknowledgments A heartfelt thanks to the EEG technicians of the Pediatric Neurology Unit: Teresa Iuorno, Carlo Landoni, Debora Meroni, Francesca Tabarelli and Gaetano Turi, for their competence and sensitivity repeatedly expressed in the management of newborns and in the acquisition of EEG recordings; to Alfredo Radaelli for his valuable collaboration in the editorial organization of the work; to the colleagues of the Neonatology and Neonatal Intensive Care of the Buzzi Hospital Milan directed by Dr G. Lista, for the useful collaboration in everyday practice.

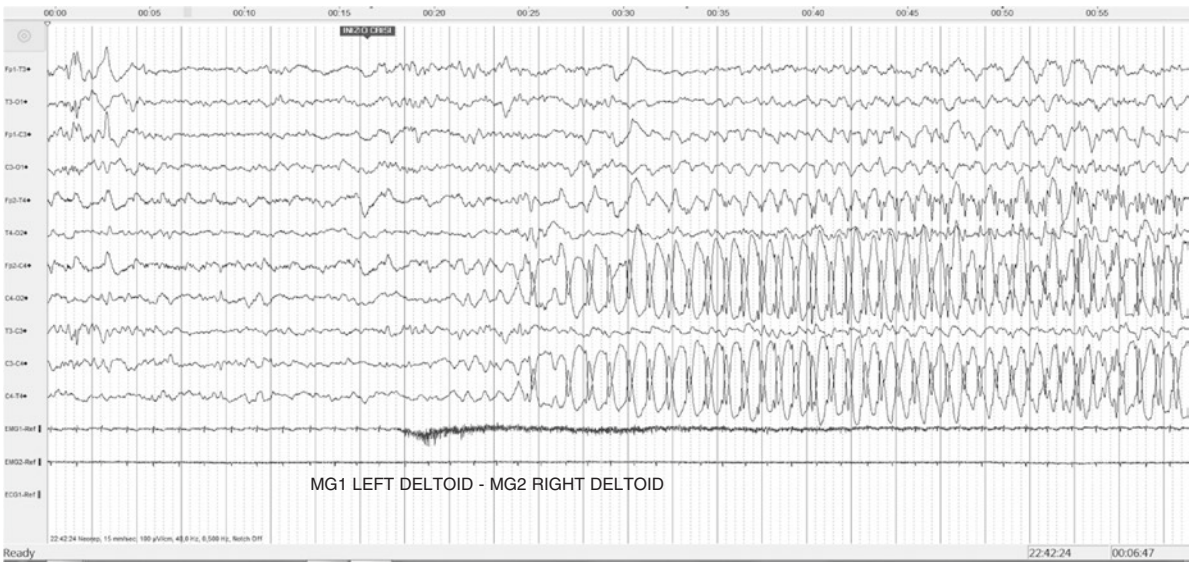

Fig. 22.66 39 weeks GA, 39.1 weeks CA. Normal pregnancy and delivery (2530 g, SGA), Apgar score 9–10. Thirty six hours after birth repetitive bilateral jerks with stiffening are referred by the nurse. An **electro-clinical focal motor tonic > clonic seizure** is recorded during the EEG performed 1 h after, an emergency. Right central rhythmic slow waves are followed by rhythmic spike-slow wave complexes high up to 250 mcV at increasing frequency with diffusion to the right temporal region: clinically the EMG polygraphy hyperactivity on the left deltoid documents the initial stiffening of the left arm. Rhythmic jerks of the left limbs follow (not shown)

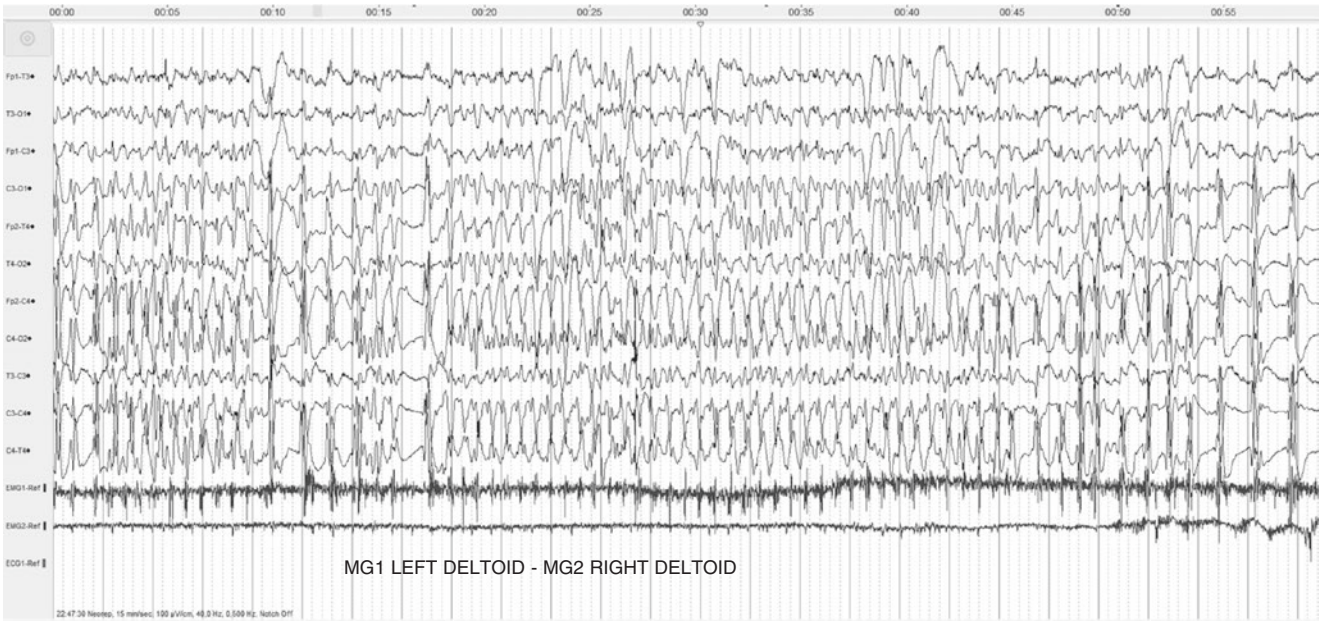

Fig. 22.67 Same newborn and same recording of Fig. 22.67). Five minutes later the ictal pattern modifies: the seizure spreads to the centro-occipital left region; polyspike-slow wave complexes are followed by transient (1 s) flattening and beta fast low-amplitude activity arises in the right occipital region; high-frequency clonic jerks of left limbs persist strictly related to the polyspikes/slow wave and spike/wave complexes. The seizure ends spontaneously within 30 s. Twenty-five minutes later a second similar seizure was recorded: after PB loading dose, 20 mg/kg, i.v. seizures never recurred. Background activity is normal in the left hemisphere. Brain ultrasound and MRI: **middle cerebral artery territory infarction**. Follow-up: normal motor and neurocognitive development at 4 years, without epilepsy, despite a poroencephalic cyst in the abovementioned region

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