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Review article

Recording conventional and amplitude-integrated EEG in neonatal intensive care unit

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ABSTRACT

Neonatal electroencephalography (EEG) presents a challenge due to its difficult interpretation that differs significantly from interpretation in older children and adolescents. Also, from the technological point of view, it is more difficult to perform and is not a standard procedure in all neonatal intensive care units (NICUs). During recent years, long-term cerebral function monitoring by the means of amplitude-integrated EEG (aEEG) has become popular in NICUs because it is easy to apply, allows real-time interpretation by the neonatologist treating the newborn, and has predictive value for outcome. On the other side, to record conventional EEG (cEEG), which is still considered the gold standard of neonatal EEG, the EEG technician should not only be well trained in performing neonatal EEG but also has to adapt to suboptimal working conditions. These issues need to be understood when approaching the neonatal cEEG in NICU and the main structure of the article is dedicated to this technique. The authors discuss the benefits of the digitalization and its positive effects on the improvement of NICU recording. The technical aspects as well as the standards for cEEG recording are described, and a section is dedicated to possible artifacts. Thereafter, alternative and concomitant use of aEEG and its benefits are briefly discussed. At the end there is a section that presents a review of our own cEEG and aEEG recordings that were chosen as the most frequently encountered patterns according to Consensus statement on the use of EEG in the intensive care unit.

Contents

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1. The influence of digitalization on NICU recordings and other technical considerations

According to the American Clinical Neurophysiology Society (ACNS) guidelines for recording clinical EEG on digital media, all laboratories need to adopt at least the minimal standards for such EEG recording.[1] The well accepted standards for digital recording of the International Federation of Clinical Neurophysiology (IFCN) should also be taken into consideration.[2] A digital EEG system converts the signal into a series of numerical values and the process is known as analog-to-digital conversion (ADC). Digital recording, reviewing and storing of the EEG data is a well established substitute for paper EEG recordings. Digital recording takes advantage of modern microprocessor computational power, costs and general flexibility. The advantages of this new technology are today widely accepted and we mention only a few: the computer software can be preset which decreases the possibility of mistakes, e.g. non-appropriate setting of filters (which were quite possible with analog EEG) and the possibility of incidental change of parameters of the record after it has been recorded (adjusting the sensitivity, speed, frequency range, etc.); the same record can be viewed in different programs or different workstations at the same time, which is considered the "magic" of the digital technology; the possibility of connecting to the internet and other network systems within the same hospital or between different hospitals (and possibility of electronic exchange of EEGs); enabling of much smaller archives (no need for large storage or microfilming); diverse possibilities of archiving (CD, DVD, magnetic tape, etc.); the possibility to burn the record on a CD and give it to the patient if he wants a second opinion; better educational abilities; and considerably smaller machines which are more suitable for recording in NICUs. The system also allows simultaneous, side-by-side display of multiple segments of EEG within one record as well as segments of different records obtained on different days, which is a perfect solution for newborn's brain electrical activity follow-up. Of course, there are drawbacks as well: the sharp shape sometimes is less obvious with digital forms; errors may happen in transmitting or archiving the data (loss of data is quite possible with just a touch of a finger); and updates of the software might render recordings of an earlier version unreadable.

In NICUs nearly all the newborns have life-threatening conditions which require many different appliances for monitoring and supporting vital functions. The technical aspects have been well established and the reader should refer to the IFCN guidelines on neonatal EEG.[3] The major factors which should be considered are: the small head circumference limiting the number of electrodes, need for polygraphic recording (to correlate the EEG with newborn's state of vigilance), longer period of recording, and more frequent follow-ups, which is particularly important for long-term prognosis.[3] The vast majority of neonates in NICU need to be intubated, sedated and may be given different muscle relaxants. The newborns are difficult to be shifted to the lab and majority of the investigations should be performed at the bedside. The above mentioned digitalization contributed to major improvements in electroencephalography so that it can be applied easily, safely and newborn-friendly in any NICU. However, the procedure is more difficult than in the neurophysiology lab and requires skilled neurophysiology assistant to be performed correctly.

The most important data to be obtained are the overall information of the functional condition of the newborn's central nervous system[4] as well as detection of any abnormality of brain electrical activity (especially seizures – clinically evident and subclinical – and differentiation from other motor non-convulsive phenomena), detection and following of their state of alertness, following the effects of treatment, and possible determining of the cause of the condition. Finally cEEG is also one of the reliable tools to determine brain death in neonates.[5,6] There are certain additional requirements for the EEG technologists in NICU as they should respect and be aware of possible interventions of the nursing staff while recording the EEG as well as possible sudden deterioration of the baby's condition (e.g., breathing problems, sudden changes in heart rate, oxygen saturation and blood pressure) and should recognize them quickly and react appropriately. He/she should also be aware of all possible artifacts caused by different procedures and devices. It is understandable also that the technician should be able to recognize all kinds of seizures: clonic, myoclonic, tonic, spasms, as well as subtle seizures associated with unusual motor and/or autonomic phenomena like pedaling, swimming, swallowing, excessive salivation, and apnoea, as well as recognizing the subclinical seizures which present only as electrographic seizure discharges on the EEG recording without any clinical signs.[7]

2. The technical standards

The standards for the cEEG recording in NICU should be the same as for routine (video) EEG recording in older infants. These should be in accordance with the standards proposed by IFCN which state that the recording in any intensive care unit should be performed by a skilled, senior neurophysiology assistant and accompanied (at least for a certain period of time) by the neurophysiologist or the person who will read the EEG.[8] This is, unfortunately, not always possible and is one of the main reasons why aEEG has become so popular in recent years.

Minimum technical standards for paediatric electroencephalography (also in NICU) were issued by the American Electroencephalographic Society[9] which specifically involve basic principles for EEG recording in young children regarding the issues of:

i the electrode application (needle electrodes are not needed and should not be used);
ii bedside recording (the technician should always consult with the nursing staff concerning the patient's condition and any limitations on recording procedures);
iii sensitivity settings (because the EEG amplitude is higher in many young children, appropriate reduction of sensitivity will be necessary – to 10 or even 15 μV/mm);
iv the length of the recording (possibly all wake/sleep cycles should be obtained: whenever possible recording the infant during wakefulness, drowsiness, initiation of sleep, natural sleep and arousal is important).

The EEG recording in neonates is well described in IFCN guidelines and many other papers; here we would like to mention two excellent reviews on EEG patterns in prematures – for normal ones by Vecchierini et al.[10] and for abnormal ones by Tich et al.[11] We would like to stress some of the more particular technical aspects for such cEEG recordings in NICU:

i channels (16-channels should be used and at least two channels should be devoted to recording of non-EEG polygraphic variables which enables the electroencephalographer to assess accurately the baby's state during the recording and to identify more reliably physiologic artifacts). Moreover, variables other than the EEG may be directly pertinent to the patient's problems, like apnoeic episodes, breathing and heart rate changes;
ii discuss the baby's condition before the bedside recording is started (absolutely essential is the gestational age and conceptional age [=gestational age + chronological age since birth] on the day of recording, stated in weeks). All other available relevant clinical information, especially current medications (sedative drugs, anticonvulsive drugs, muscle relaxants, respiratory stimulants, antiarrhythmic drugs, etc.) should be noted for the electroencephalographer's use;
iii time of recording (it is advantageous to schedule the EEG at feeding time and arrange to feed the baby after the electrodes have been applied, but before beginning the recording). Allow for extra recording time for the EEGs in neonates as the time is commonly lost due to a greater number of movement and other physiologic artifacts and usually more time is needed to obtain sufficient recording to permit evaluation of stages of the wake-sleep cycle and other states. It may be necessary to obtain a 45–60 min long recording if the pattern appears to be invariant, to demonstrate that the tracing is not likely to change. Be also aware that initial sleep in neonate and young infant is usually active sleep, which may last very short time – an adequate sleep tracing must include a full episode of quiet sleep. However, repetitive photic stimulation is rarely, if ever, clinically useful in neonates and is not recommended;
iv the baby's condition (head and eyelid position) should be clearly indicated at the beginning of every montage. Continuous observation by the skilled technologist, with some experiences in newborns' behavior, with frequent notations on the recording is particularly important. In stuporous or comatose newborns and in those displaying invariant EEG patterns, visual, auditory and somatosensory stimuli should be applied systematically during recording, but only toward the end of the recording period so that the minimum of the normal sleep cycles be disrupted and/or to prevent possible unexpected arousal-produced artifacts which would render the tracings unreadable thereafter. The stimuli and the newborn's clinical responses or failure to respond should be noted on the recording as near as possible to their point of recurrence;
v the most suitable cap size is usually used, however, if there are any bruises or needles on the newborn's head, the electrodes should be glued. The position of the electrodes and the impedance should be checked during the recording as the newborns may move. If the parents are present we should explain them everything about the preparation of the baby and the recording itself;
vi additional sedation is usually not necessary, however, sometimes low dose of chloral-hydrate or even better, melatonin should be used. Recently it has been shown that the shorter sleep duration and drowsiness period were the two advantages of melatonin over chloral-hydrate and also there has been higher yield of seizure activity detection in melatonin sedated patients, so that authors concluded that melatonin was in favor of its prescription for sleep EEG recording in the paediatric population.[12]

The *artifacts* in the cEEG recording while the baby is in NICU are quite common. In ideal conditions the electroencephalograph should be without any technical failures, grounding and electricity setting in the NICU should be perfectly done. The ideal temperature, humidity, lightening and silence should be achieved. The movement artifacts due to movement of the staff should be minimalised. The staff should also take care of the newborn's airways to be properly cleaned. If any urgent procedures are needed during the recording, the technician should be informed on time about these (of course, some urgent procedures can not be precluded in life-threatening conditions), so that he/she can note the exact time of such procedures. We should also be aware that besides brain electrical activity some non-cerebral activity could also be recorded, such as electrical biological signals due to sweating, muscular activity, body movements or ocular movements. Some biological signals will be difficult to exclude, such as heart rhythm and the so-called ballistocardiogram (especially when the brain electrical activity is low and sensitivity is therefore increased). Finally there are also artifacts from power lines and equipment (intravenous drip – infusion pump, heaters of the incubators and beds), from electromagnetic interference (signals from nearby monitors, television, telephones, cardiac pacemakers) and electrostatic artifacts, which can be produced by a person walking through. Such artifacts in a busy intensive care unit can be avoided to some extent if the infant's head and the connections of the cEEG machine can be kept as far as possible from the power cables and electrical equipment. All possible interferences and artifacts should be noted in the record.[13]

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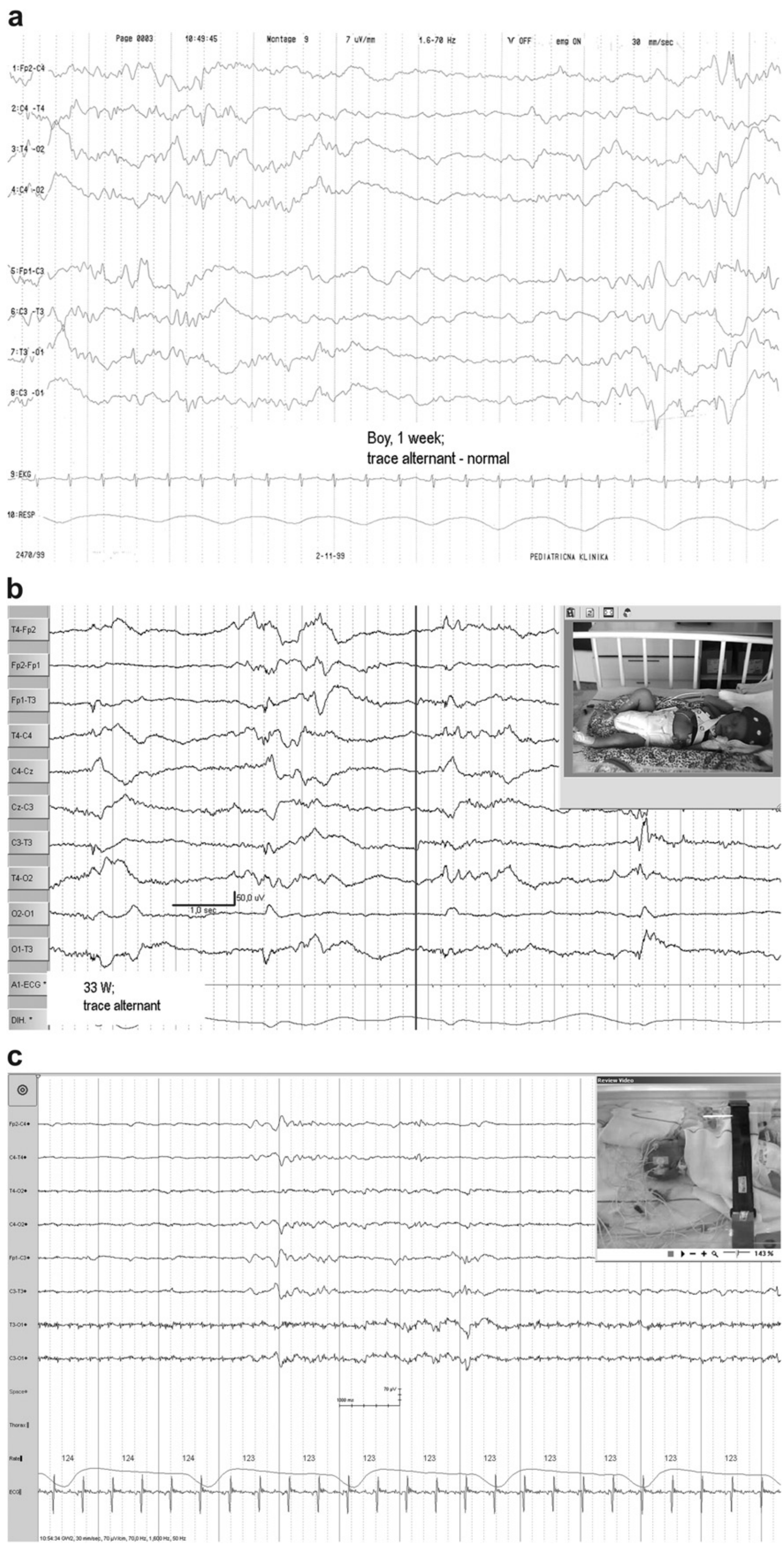

Fig. 1 – **Normal *tracé alternant* pattern in a one-week-old newborn. Presented is a period of slow and sharp high-amplitude background activity (BA) followed by low-amplitude BA and again high-amplitude BA (a). Sometime the same pattern can be found already at 33 weeks of gestational period (b), and still resembling so-called *tracé discontinue* pattern of the preterm of between 31 and 32 weeks of gestation (c). This and all the other recordings are performed at sensitivity 1 cm = 70 μV.**

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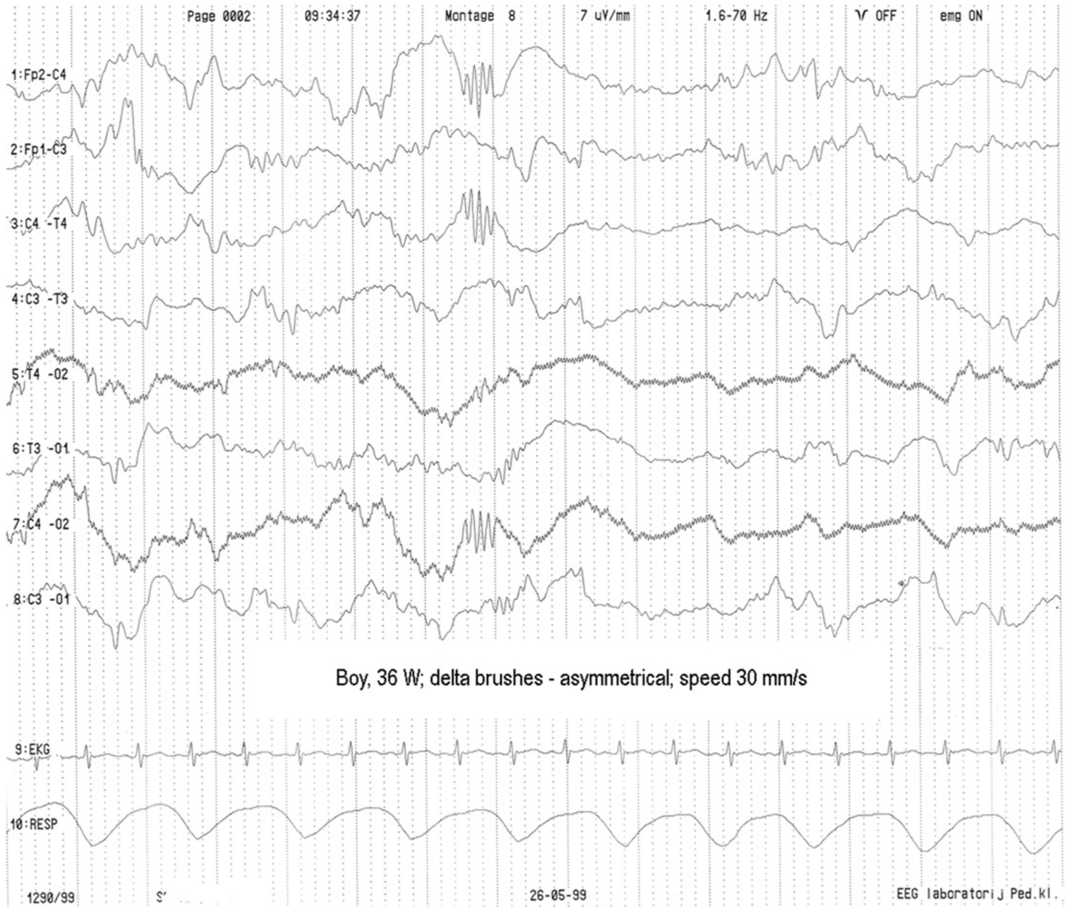

Fig. 2 – Asymmetry of delta brushes in a preterm during quite sleep. This infant has had a completely normal outcome.

For prognostic purposes it is recommended to do at least two recordings, best separated by 24 h.[14]

Finally, if possible and if available also in clinical settings (not only for research purposes) it is very useful if cEEG recording and aEEG can be performed simultaneously.

Long-term monitoring of brain function with aEEG has become part of the routine neurological care in the neonatal unit in the last two decades. It has been used for assessment of background pattern, detection of seizures, evaluation of the effects of anticonvulsive drugs, selection of patients for neuroprotective intervention, and prediction of neurodevelopmental outcome as early as in the first hours after birth.[15] With the increased use of aEEG, concerns have been raised about the accuracy and reliability of the interpretation of aEEG by clinicians, but its prognostic value after birth asphyxia is well established.[16] Modern digital monitors provide the unprocessed EEG signal as well as the aEEG from 1 or 2 channels. The unprocessed EEG signals used together with aEEG may improve electrical seizure detection,[17] which is particularly useful as a large proportion of neonatal seizures are subclinical, especially after administration of antiepileptic drugs.[18] A substantial body of evidence now exists, that treating subclinical seizures in neonates might improve their outcome.[19] Some of the newer aEEG devices also provide automatic seizure detection, which even further simplifies the interpretation of aEEG. Bourez-Swart et al. have recently shown that even a single-channel aEEG may help identify most newborns with severe neonatal seizure patterns (including those with frequent subclinical seizures) with the sensitivity of 92%, however, the use of multiple channels as with the cEEG, results in identification of *all* patients with seizure patterns.[20] Although cEEG remains the gold standard of neonatal EEG, aEEG is a great tool for long-term monitoring of newborn's brain function and can provide valuable information to the clinician.

3. Some possible scenarios in NICU: from normal to abnormal recordings

The usefulness of EEG in intensive care unit has been brilliantly documented in the "Consensus paper".[21] We will just use some of its conclusions as a base to illustrate some of our own recordings:

i in premature neonates deep brain lesions (like periventricular leucomalacia) may cause the disappearance of normal maturational features and/or occurrence of positive sharp waves over central (rolandic) regions – PRSW;

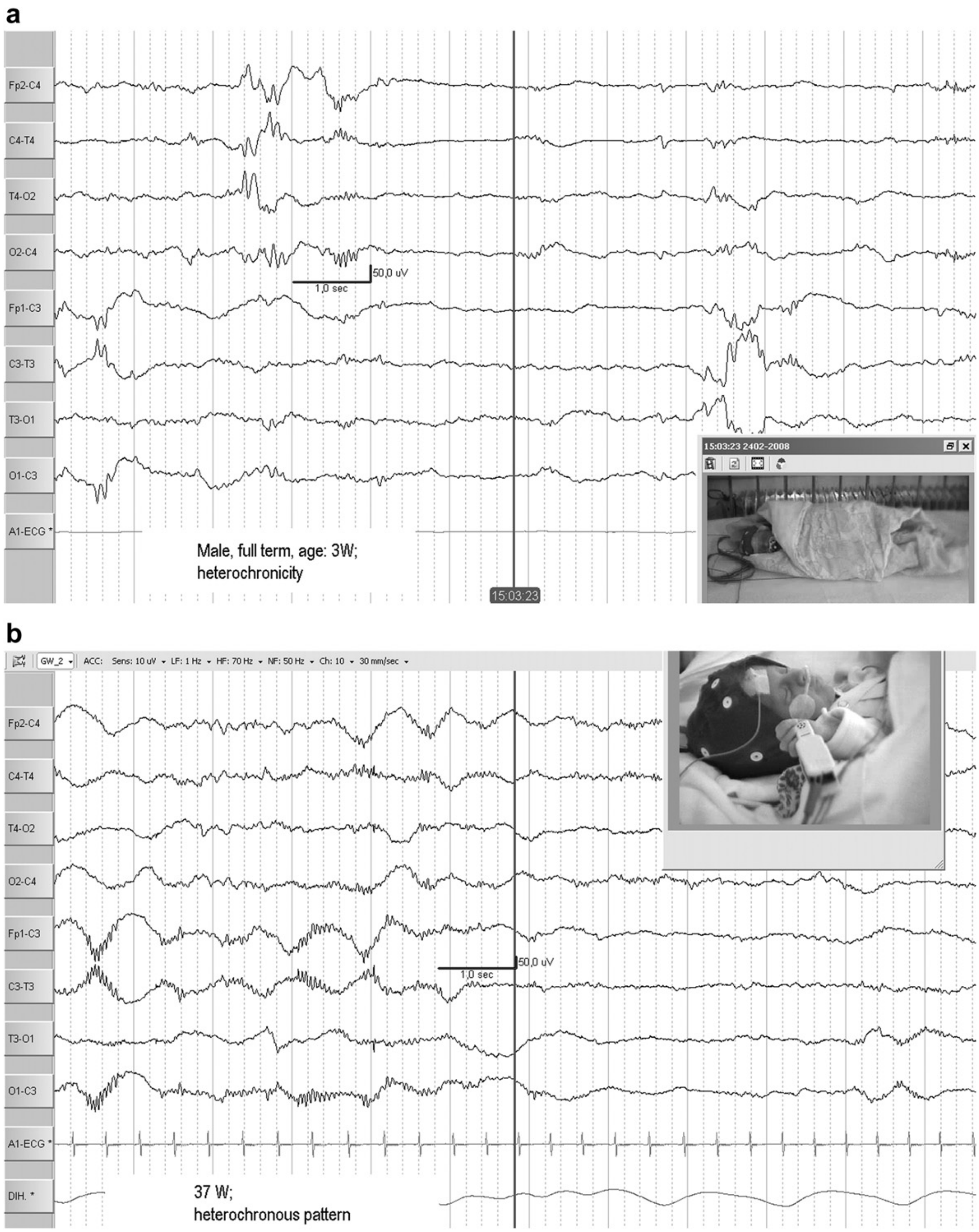

Fig. 3 – Two different heterochronous patterns (clearly visible delta brushes) in two different full-term newborns, who later showed severe intellectual disability (a) and encephalopathy with cerebral palsy (b).

ii in term neonates, however, the most frequent abnormalities are due to cortical dysfunction: abnormalities of background EEG pattern, neonatal seizure discharges and periodic lateralized electrical discharges (PLEDs as well as multifocal rolandic and/or temporal sharp waves due to deeper lesions;

iii special attention should be given to clinically silent seizure discharges which can be harmful and should be treated;

iv regarding the prognosis there are some general rules that should be taken into account: EEG patterns that carry an ominous prognosis are electroclinical silence irrespective of age (in the absence of sedative drugs) and burst-suppression pattern in those older than 32 weeks of CA. Normal cEEG recordings are generally related to good outcome.[14] Intermediate EEG patterns justify serial recordings.

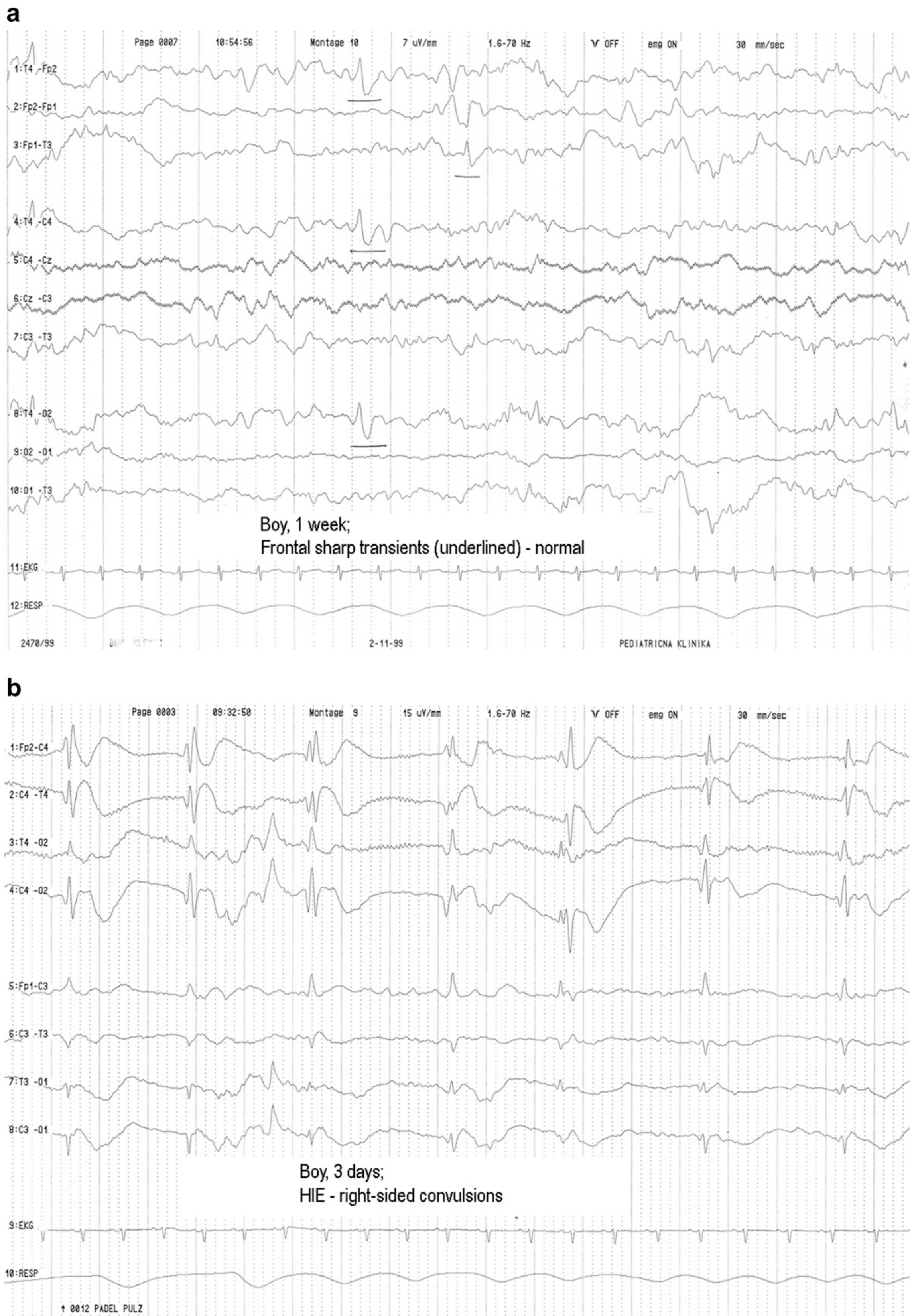

Fig. 4 – (a). Physiological *frontal sharp transients* (biphasic sharp waves - underlined) are typical pattern of a newborn during so-called active sleep. This newborn has had normal outcome at age of one year. (b). This EEG reveals high-amplitude sharp waves and spikes, localized to the right hemisphere (first four derivations) – clinically ipsilateral clonic seizures in a newborn with brain hypoxia were observed. Signs of moderate cerebral palsy – left-sided hemiplegia - in the second year of life.

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Some of these conclusions are presented as possible scenarios in NICU. Conventional EEG is traditionally based on visual interpretation of criteria ("gestalt" perception) that usually include at least: continuity/discontinuity, amplitude – especially its symmetry, interhemispheric synchrony, lability to behavioral states and background EEG composition.[22,23] One of the most characteristic features of newborn EEG is its discontinuity where during quiet sleep high-amplitude bursts are intermingled with low-amplitude interburst intervals, giving the typical pattern of *tracé alternant*. This pattern is a physiological one and is present in all newborns around 35 weeks of postconceptional age and persists until 44–46 weeks of postconceptional age (Fig. 1). While the symmetry of background activity is a must in infants and older children, in newborns 20%–30% of asymmetry is still acceptable, especially when asymmetry of otherwise physiological graphoelements is seen (e.g. asymmetry of *delta brushes* in preterms or asymmetry of *frontal sharp transients* in full-terms – Fig. 2). Asynchrony means a time-frame shift of appearance of certain graphoelements, rhythms and bursts e.g. when sleep spindles in infants appear first over one hemisphere only and then after few seconds also over the other one. Some degree of asynchrony is quite acceptable up to the age of 6–12 months. Lability means background changes through the whole record, while composition of EEG background activity changes with maturation and means that certain graphoelements will prevail and be characteristic for certain postconceptional ages (e.g. delta brushes in preterms of 32–35 weeks of postconceptional age). If these same patterns were still present at later ages (near-term), this is labeled as heterochronicity or dysmaturity of EEG features (presence of EEG pattern that is two or more weeks immature) compared to the corrected age (Fig. 3) and such visual interpretation can be divided or subdivided into certain categories like: mildly, moderately and markedly (severely) heterochronous recordings.[24] If we can perform serial or multiple EEGs within first few weeks of life, persistence of such abnormalities can not only confirm the diagnosis of severe brain damage but also prognosticate unfavorable outcome. Some authors even distinguish between such abnormal patterns that are consistent with cerebral palsy and those that are more associated with future mental retardation.[25] It should not be difficult to distinguish between physiological graphoelements (e.g. sharp frontal transients) (Fig. 4a) and clear electrographic spikes (Fig. 4b) and to detect *positive rolandic sharp waves* in newborns with either intracranial hemorrhage or, even more frequently, periventricular leukomalacia,[26] which may (especially when persisting) be prognostic of future cerebral palsy (Fig. 5).

4. Electrocerebral inactivity and burst-suppression pattern

These are the most severe types of neonatal brain activity abnormalities. Inactivity or *electrocerebral silence* is defined as no EEG activity over 2 μV/mm when recording from scalp

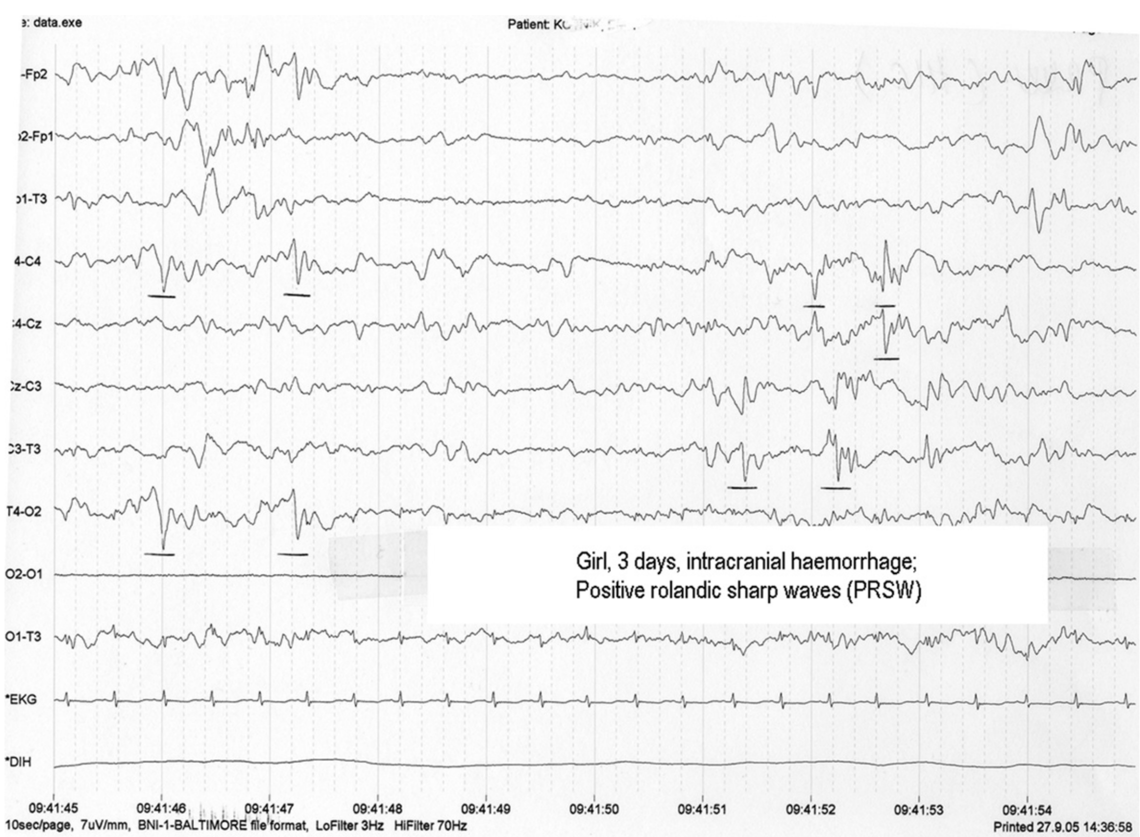

Fig. 5 – Characteristic positive (downward) sharp waves over central (rolandic) areas in a female newborn with grade III intracranial haemorrhage (so-called *positive rolandic sharp waves*) – PRSW. Mild cerebral palsy (level I) at the age of two years.

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electrode pairs 10 or more cm apart for at least 30 min.[9,27] Due to immaturity and relative resilience of the neonatal brain it is often recommended that a second EEG should be obtained several days after the first one to rule out a transient phenomenon. Although we are aware that aEEG has replaced the cEEG for continuous monitoring of cerebral function in many tertiary care units, especially for monitoring severely asphyxiated newborns, there is no data to support the use of aEEG for assessment of brain death in neonates.

A *burst-suppression pattern* is characterized by periods of excessively suppressed background activity (less than 5 μV) intermingled with bursts of abnormal activity. It is essential that such a pattern would not be confused with the normal EEG pattern (*tracé discontinu* or *tracé alternant*) of prematurity (Figs. 1 and 6). This pathological pattern shows no lability to behavioral states, is not reactive to stimulus, burst to inter-burts intervals are usually fixed and, in the most severe cases, the interburst intervals usual exceed 30 s. In such conditions, according to our own experiences, and data from the literature, the best results can be achieved if we combine both aEEG and cEEG.[13,28–30]

In those instances where, according to aEEG result, one is not sure about such a tracing, concomitant cEEG tracing can clearly confirm such a fact (Fig. 7a and b). The majority of neonates who present this cEEG or aEEG pattern for prolonged periods of time have poor psychomotor prognosis.[16,31]

5. Seizure discharge patterns

Seizures are difficult to diagnose clinically in preterm as well as in term newborns. It is quite often that clinical paroxysms have no electrographic correlate and maybe even more often that paroxysmal electrographic seizure discharges that lack clinical correlate occur on cEEG or aEEG,[20,32]. Like all electrographic seizure discharges, neonatal ones also have a definite beginning and rather clear ending. Such features are very useful to distinguish ictal rhythmic discharges from artifacts (Fig. 8). EEG definitions vary but paroxysms are considered seizures if they last at least 10 s and are not sustained, while longer seizure duration (>60 s) was associated with poor outcome.[20] Here it should be mentioned that short lasting seizures would be represented by very brief aEEG deflection, e.g. if the typical displayed speed is 6 cm/h, and the median duration of seizures would be 60 s, an aEEG deflection will only be 1 mm. The detection of seizures with an aEEG tracing also requires the seizure amplitude to be quite higher than the EEG background, while common 2:1 ratio of ictal to interictal peak-to-peak amplitudes may prove to be too low to produce consistently discernible deflections on the aEEG.[30] If the discharges are less than 10 s duration they are described as brief (interictal) rhythmic discharges (BRDs or BIRDs) and are of uncertain significance while it has been described that subsequent EEGs with BIRDs may be associated with electrographic neonatal seizures and impaired neurodevelopmental outcome.[33] The same authors have shown that the presence of BIRDs was significantly associated with leukomalacia and hypoglycemia in the cross-sectional analysis of baseline data. There was an increased risk for abnormal neurodevelopmental outcome after a mean follow-up period of 47 months. Consequently they stressed the need to include these brief episodes in future studies of neonatal seizures. Neonatal seizure discharges often have a focal onset, even if they present simultaneously as independent foci (seizures can

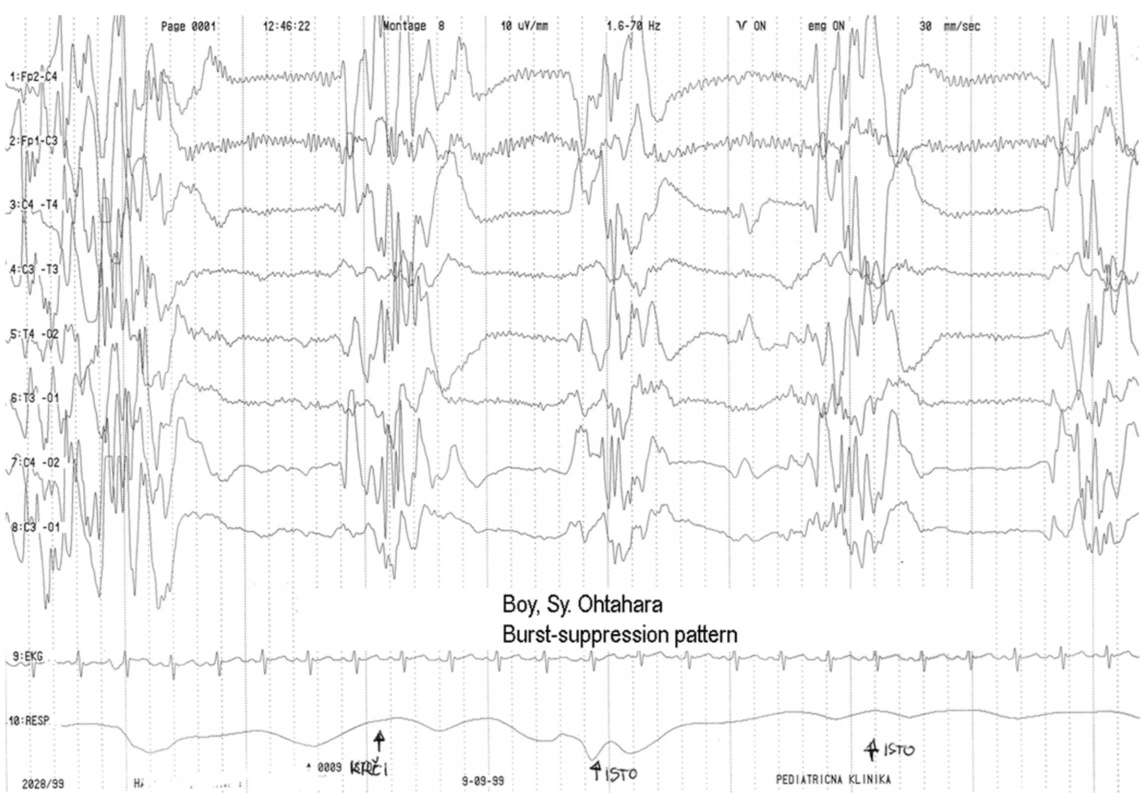

Fig. 6 – Obvious burst-suppression pattern which should be distinguished from *tracé alternant* pattern (see also Fig. 1).

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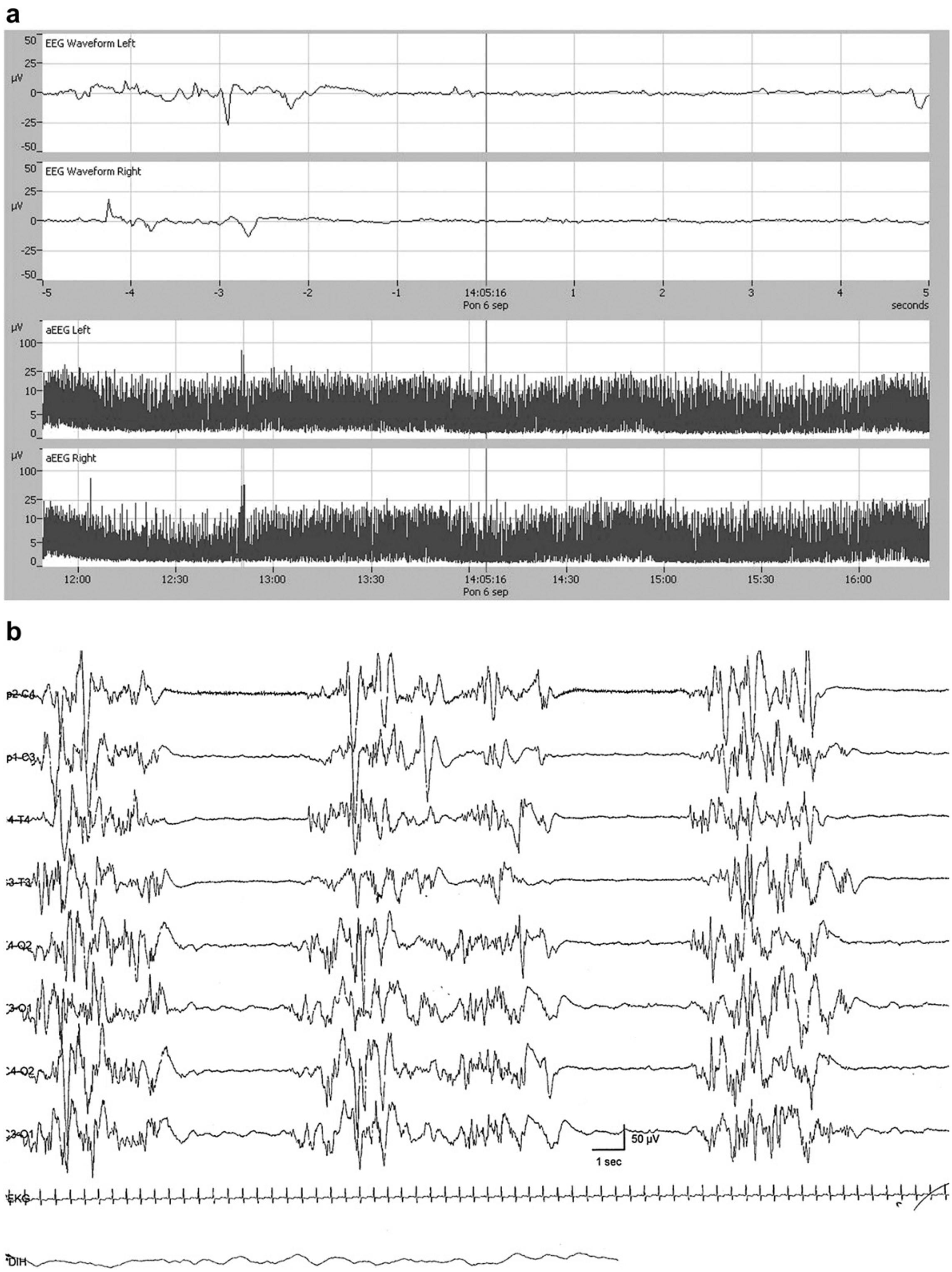

Fig. 7 – When suspicious burst-suppression pattern is found on aEEG (a), the best results can be achieved if we combine it with the standard EEG, which will clearly confirm such a fact (b).

originate persistently from one part of the brain – unifocal, or arise from multiple parts - multifocal), while generalized seizure discharges are rare. The study of Shellhaas and Clancy[30] revealed that almost one fifth of the seizures started in frontal and occipital areas and less than half of these were reflected at the C3–C4 derivation, which suggested that it might not be rare to have newborn whose seizures are not seen at all in a single derivation. Persistent unifocal seizures are suggestive of an underlying structural lesion or may confirm some typical neuroimaging finding such as

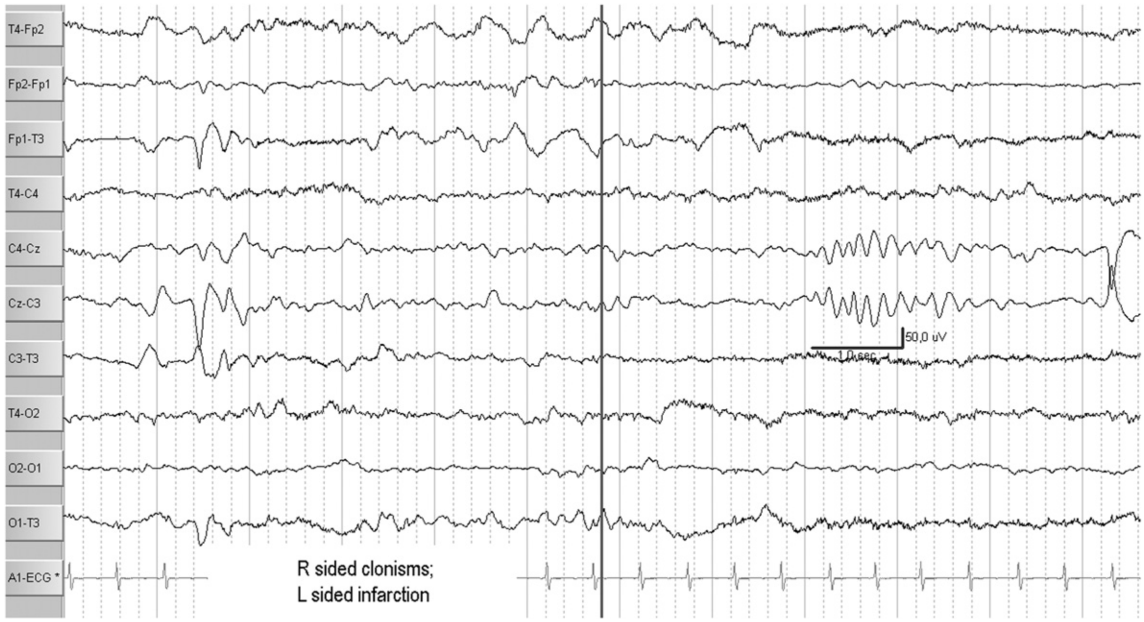

Fig. 8 – Rather sharp start and ending of rhyhmic discharges (over Rt and Lt central areas: C4-Cz and Cz-C3 electrodes) in a newborn who later was found to have Rt–sided congenital haemiplegia due to neonatal brain infarction.

intracranial hemorrhage;[34] (see also Figs. 4b and 5). The morphology can vary from simple sharp waves to polyspikes and even some alpha-like spindles, and can be of different frequencies (from delta to beta range). Usually they will increase in the amplitude and frequency if the seizure discharges are more sustained.

6. Summary

Recent advances in neonatal neuroimaging have been accompanied by marked improvements in recording brain electrical activity. Digitalization and video synchronization of the cEEG recording as well as the introduction of the aEEG into clinical practice in NICU have proven to be particularly useful. The cEEG remains the technique of choice for the functional investigation of the neonatal brain. Common pathophysiological processes, such as brain hypoxia-ischaemia, raised intracranial pressure, infectious and metabolic changes, and seizures will be reflected on the cEEG and should be skillfully interpreted.[35] Only good technical standards with all the above mentioned properties and good understanding of the underlying clinical problem will allow a good, reliable and fast interpretation of the cEEG as well as aEEG recording in the NICU.

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