Paediatr Croat 2008;52:125-130

ZNANSTVENI PREGLED
SCIENTIFIC REVIEW

UDK 616-053.4; 616-073

DIAGNOSTIC POSSIBILITIES OF VIDEO-ELECTROENCEPHALOGRAPHY AND AMPLITUDE-INTEGRATED ELECTROENCEPHALOGRAPHY DURING EARLY LIFE

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The main aim in managing sick newborns is to prevent or at least to minimize brain injury and to establish optimal neuro-developmental outcome. Electroencephalography (EEG) which reflects brain electrical activity, is regarded as the most reliable tool in recognition of possible central nervous system dysfunction (e. g. seizures) and in predicting outcome. The best surveillance of a neonate and young infant can be achieved by continuous functional monitoring, but long term EEG has limited availability in many centres and requires interpretation by a skilled paediatric electroencepahlographist. Therefore, amplitude-integrated EEG (aEEG) is a technique for simplified EEG monitoring which has an increasing clinical potential in neonatal intensive care. The article presents literature data as well as our own experience with diagnostic possibilities of both, standard (digitalized and video-assisted) EEG as well as aEEG and stresses the importance of using new generation machines that incorporate, along with aEEG signal, also a display of raw EEG for better seizure detection.

Descriptors: ELECTROENCEPHALOGRAPHY – methods; VIDEO RECORDING; INTENSIVE CARE, NEONATAL – methods; SEIZURES – diagnosis; BRAIN DISEASES – diagnosis; HYPOXIA-ISCHEMIA, BRAIN - diagnosis

INTRODUCTION

At our Department of Child, Adolescent and Developmental Neurology in Ljubljana University Children's Hospital we have been using electroencephalography (EEG) since year 1954 when the first EEG machine (even the first one in whole former Yugoslavia) had been introduced at our department by Professor

Jože Jeras (1). The machine was produced by Eden and has been bought by donation from American Women's Association (the practice that machines are bought from donations is still employed in present times) and has been used for more than 20 years as a supplementary diagnostic tool for clinical follow-up of children and adolescents with epilepsy. Such good clinical and EEG diagnostics and their correlation enabled professor Jeras and his co-worker Ivica Tivadar, MD to write the first textbook on Epilepsies in children in the English language (2). At the end of the 1990s a non-governmental organisation was established to help the department (Foundation of Child Neurology (http://pednevro.pedkl.si/si/ustanova/) and this enabled us to buy the most sophisticated digital machines for EEG. One after another the following techniques for EEG registration in newborns, infants, children and adolescents were introduced: digital EEG, digital video EEG, ambulatory EEG, ambulatory polysomnography, videotelemetry (bought by League aginst Epilepsy, Slovenia). The machines were first produced by Oxford-Medelec, thereafter by Nicolet but then both companies merged and now the joined group is called Viasys. Such excellent electrophysiological possibilities enabled us to publish a series of booklets aimed at better basic knowledge of different neurophysiological techniques for adults and children and they are all collected in one book (3) and available free at: http://pednevro.pedkl.si/wp-content/uploads/2008/07/EEG_book.pdf.

Amplitude-integrated EEG (aEEG) is a technique for one- or two-channel EEG monitoring that is increasingly used in neonatal intensive care units (NICU). The first cerebral function monitor for aEEG was designed in the 1960s by Maynard and applied in adult intensive care by Prior. In neonatology it has started to play an important role when considering therapeutic possibilities in infants with perinatal hypoxia. The best practical guidelines as well as classification and interpretation for newborns and preterm babies have been given by al Naqeeb et al (4), Rosen (5) and Hell-

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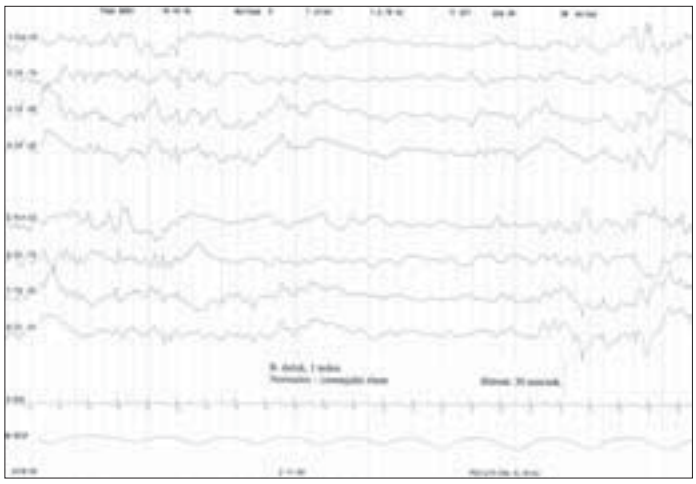

Figure 1. *Normal tracé alternant pattern in a one-week-old newborn. Presented is a period of slow and sharp high-amplitude background activity (BA) followed by low-amplitude BA and again high-amplitude BA.*
Slika 1. *Primjer normalnog tracé alternant obrasca cerebralne aktivnosti u novorođenčeta u dobi od jednog tjedna. Prikazana je osnovna cerebralna aktivnost u vidu nizova sporih i oštrih valova visokih amplituda koje slijede naizmjenično nizovi valova niskih i visokih amplituda.*

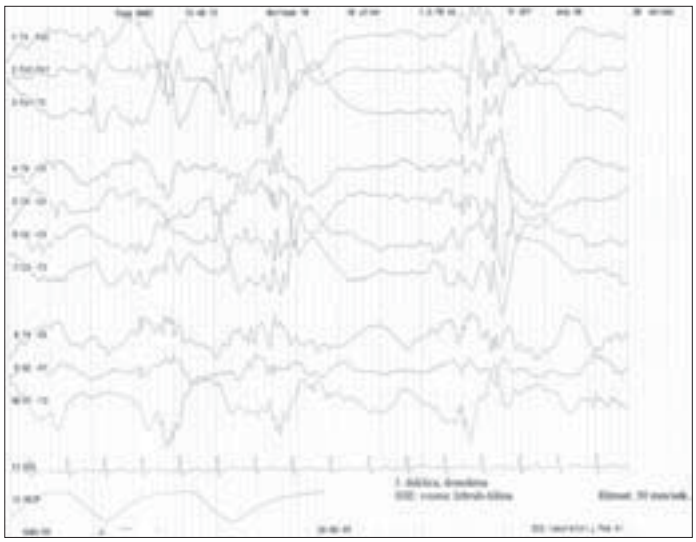

Figure 2. *In comparisson with the physiological pattern of tracé alternant this record presents a clear-cut low amplitude BA period (in the centre) with bilateral bursts of high-amplitude sharp waves and spike & wave complexes. This is a characteristic pattern of hypoxic-ischaemic encephalopathy (so called burst-suppression pattern).*
Slika 2. *Za razliku od fiziološkog oblika tracé alternant ovaj snimak pokazuje odsječak niskovoltažne osnovne cerebralne aktivnosti (u sredini) s bilateralnim izbijanjima visokovoltažnih oštrih valova i šiljak – val kompleksa. Ovo je karakterističan oblik hipoksičko – ishemičke encefalopatije (takozvani obrazac burst-suppression aktivnosti).*

ström–Westas et al (6). Soon after the last »revival« of aEEG technique we also had our first experiences in aEEG of neonates. These first steps resulted in the PhD thesis of one of us (D. O.) in 2006 (7). The first machine we used still used paper (Lectromed) and were introduced into everyday clinical practice at departments of Neonatology, Child Neurology and Pediatric Surgery and intensive care - NICU. About five years ago new machines were introduced which were not only completely digitalized but also have integrated raw EEG signal (Brainz monitor and NicoletOne monitor). They enable simultaneous registration of several channels of standard EEG and can even completely substitute standard EEG recording in newborns and infants (NicoletOne). However, aEEGmonitor has no simultaneous video recording and classical videoEEG is still considered the gold standard for electrographic seizure detection and quantification (8). There are many reports in the literature about the use of aEEG in cases of hypoxic-ischaemic encephalopathy - as an excellent tool to assess the current status of a neonate, for decision about further diagnostic possibilities, as well as to predict further neurodevelopmental outcome (9, 10), and especially risk for development of postneonatal epilepsy (11). Monitoring of cerebral functions also played an important role in multicenter neonatal neuroprotective trials of selective head cooling versus full-body cooling and predicting outcome of neonates with neonatal encephalopathy (12), while it is being evaluated as a diagnostic tool for other disease entities encountered in an intensive care setting (13, 14).

We will present some of the most frequent uses of classical EEG (associated by video) as well as aEEG.

CLASSICAL DIGITAL EEG WITH CONCOMITTANT VIDEO RECORDING (VIDEOEEG)

Classical EEG is traditionally based on visual interpretation of criteria (*»gestalt«*) that usually include at least: continuity/discontinuity, amplitude – especially its symmetry and synchrony, lability to behavioral states and background EEG composition (15). 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 to 46 weeks of postconceptional age (figure 1). However this pattern (especially when higher amplitudes are intermingled) is frequently confused with one of the most pathological ones – pattern of *burst-supression*, which usually accompanies moderate to severe hypoxic brain insult (figure 2). In such a situation when we are not sure whether we are dealing with a normal pattern or a severely abnormal one, simultaneous video recording can be of great help; in the first instance the neonate (or preterm) will be quietly sleeping, while in another video it may demonstrate a comatose or even convulsing, severely ill newborn. While the symmetry of background activity is a must in infants and older children, in newborns 20% to 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 – figure 3). Asynchrony means just time-frame shift of appearance of certain graphoelements 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 and composition of EEG background activity mean 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). Such visual interpretation can be divided or subdivided into certain categories like normal and abnormal: mildly, moderately and markedly (severely). If we can perform serial or multiple EEGs within the first few weeks of life, the persistence of such abnormalities may not only confirm the diagnosis of

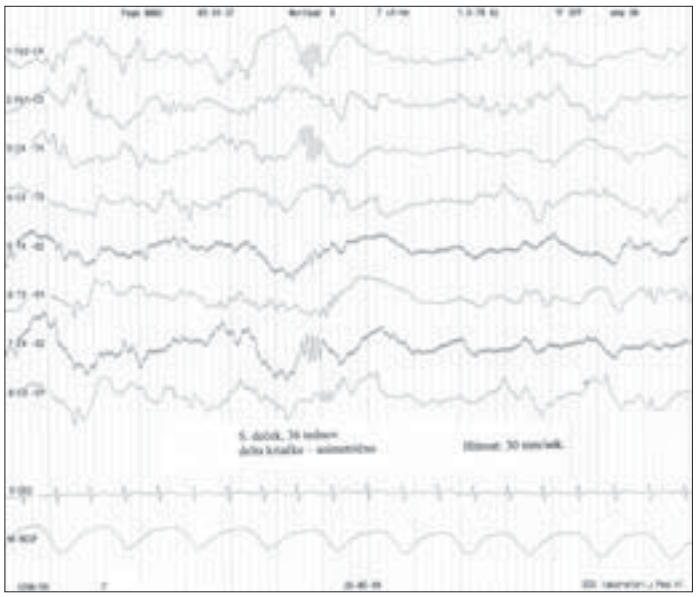

Figure 3. *Asymmetrical delta brushes (superimposed fast and sharp rhythms on delta waves) were considered as normal on this recording, despite the asymmetrical appearance. This newborn has had completely normal neurodevelopmental outcome at one year of age.*
Slika 3. *Asimetrična delta aktivnosti (sa superponiranim brzim ritmičkim ritmovima) bila je procijenjena kao normalan nalaz u ovom snimku, osim asimetričnog izgleda. Ovo novorođenče je imalo potpuno uredan neurorazvoj u dobi od jedne godine.*

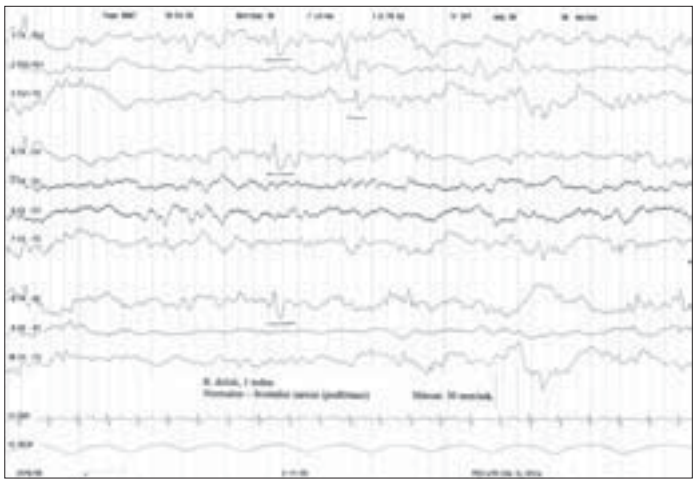

Figure 4. *Physiological frontal sharp transients (biphasic sharp waves) are typical pattern of a newborn during so-called active sleep. This newborn has had normal outcome at age of one year.*
Slika 4. *Fiziološka pojava pojedinačnih oštrih aktivnosti (bifazični oštri valovi) tipičan su oblik u novorođenčeta u aktivnom spavanju. Ovo novorođenče je imalo normalan razvoj u dobi od jedne godine.*

severe brain damage but also prognosticate unfavourable 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 (16). However, the most important diagnostic role of video EEG during early life is still in its possibility to detect clinical, subtle as well as electrographic-only seizures. It has been well documented that the specificity and sensitivity of EEG for seizure detection are at the highest level during the neonatal period, with one obligatory condition – the EEG recording must be read by an experienced reader of neonatal EEG. Sometimes it is not difficult to distinguish between physiological graphoelements (e .g. sharp frontal transients) (figure 4) and clear electrographic spikes (figure 5). Sometimes we can also find specific graphoelements of certain abnormal conditions (e. g. repetitive temporal spikes in herpetic encephalitis) during the neonatal period, such as so called *positive rolandic sharp waves* which are representative of either intracranial haemorrhage or, even more frequently, periventricular leukomalacia, which may (especially when persisting) prognosticate future cerebral palsy (figure 6).

When video and especially serial video EEG are introduced into neonatal electroencephalography, the positive predic-

Figure 5. *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.*
Slika 5. *Ovaj EEG pokazuje oštre valove i šiljke visokih amplituda, lokalizirane na desnoj hemisferi (prva četiri odvoda) - u novorođenčeta s moždanom hipoksijom uočeni su ipsilateralni klonički napadaji. Znaci cerebralne paralize – ljevostrana hemiplegija u dobi od dvije godine.*

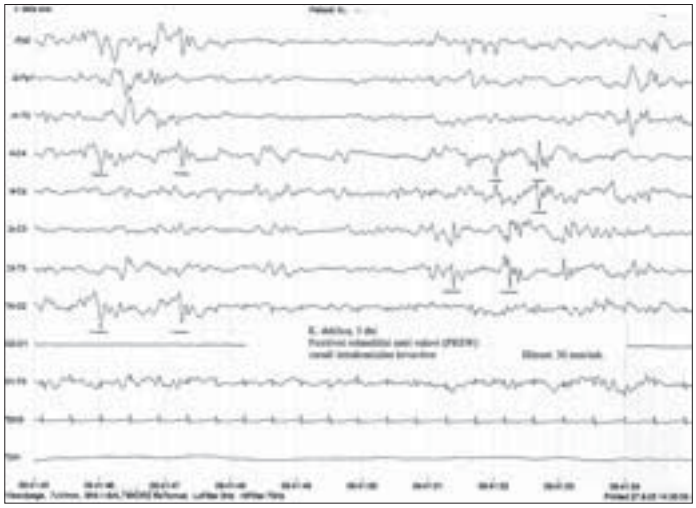

Figure 6. *Characteristic positive (downward) sharp waves over central (rolandic) areas in a female newborn with grade III intracranial haemorrhage (so called positive rolandic sharp waves – PRSW). Mild cerebral palsy (level I) at the age of two years.*
Slika 6. *Karakteristični pozitivni (prema dolje usmjereni) oštri valovi preko centralnih (rolandičkih) regija u ženskog novorođenčeta s intrakranijalnim krvarenjem III. stupnja (tzv. pozitivni rolandički šiljak-valovi). Blaga cerebralna paraliza (stupanj I.) u dobi od dvije godine.*

a)

b)

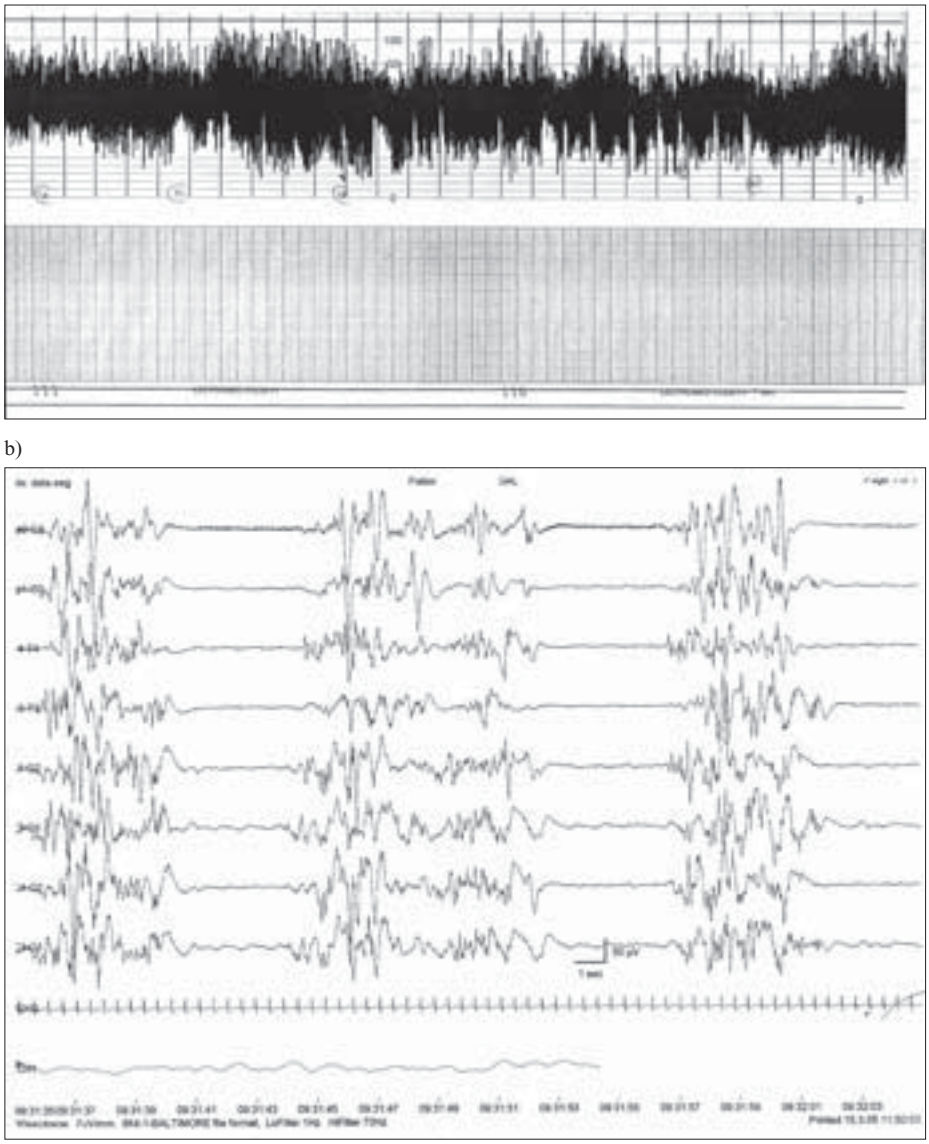

Figure 7. *Burst-suppression pattern was suspected by aEEG (7a) in this case and confirmed by standard EEG (7b).*
Slika 7. *Burst suppression oblik aktivnosti bio je sumnjiv na aEEG-u (7a) i potrvrđen na standardnom EEG-u (7b)*

tive value for seizures become even higher because now a higher percentage of subtle seizures can be detected and treated accordingly (17). But limited availability of expensive technology and professional staff on the one hand and the technical challenges on the other are some of the major reasons why, especially during the last decade, an alternative method has become so popular –cerebral function monitoring.

CEREBRAL FUNCTION MONITORING BY AMPLITUDE-INTEGRATED ELECTROENCEPALOGRAPHY (AEEG)

Many authors have found aEEG to have an excellent predictive value for neurodevelopmental outcome in newborns with hypoxic-ischaemic encephalopathy (9, 12, 18, 19). This holds true especially for cases of moderate and severe hypoxic-ischaemic brain damage. However, in one case series we also found that aEEG can be quite a reliable tool for assessment of the risk for brain damage in newborns without the need for ventilatory support (20). In a recent study by Shany et al., which included, besides their own, also four other similar and comparable studies, it has been confirmed that significantly abnormal patterns, such as flat tracings or very low voltage and so-called burst-suppression pattern are highly predictive for later neuro-developmental outcome (12). Positive predictive value was between 69% and 86%, while sensitivity was between 75% and 100%. The interpretation of aEEG is simple and reliable and it has been proven to correlate well between different profiles (e. g. medical students, NICU nurses, child neurologists), however, it is of utmost importance that cerebral function monitoring is done early during the neonatal period, the best within first 3 – 6 hours of life (21). Monitoring asphyxiated infants with aEEG (and possibly also by standard EEG or by combination of both) is becoming an accepted practice in many NICUs and is recognized by some authors as most probably the best or at least a very important tool to select patients for various neuroprotective studies, and is on the other hand also a fantastic tool to identify those newborns with good outcome which may help to reduce the anxiety of parents at an early stage (12). aEEG has also been found to be an excellent tool for detecting seizures, especially clinically silent ones. Electroencephalographic seizures are common in severely-ill newborns and aEEG may provide important information concerning their neurological status and may help to confirm or refute the presence of seizures in clinically suspected cases and detect infants with silent seizures (13, 14). It has also been shown that early detection and treatment of clinical or subtle or just electrographic neonatal seizures by aEEG is of great importance as the incidence of postneonatal epilepsy after early institution of treatment was only 9.4% which is lower than usually reported in the literature (11). We have also shown recently that aEEG can be successfully used for other conditions in sick newborns treated at NICU, e. g. for those neonates who are treated by extracorporeal membrane oxygenation, because aEEG in such cases also provides additional data which can be used for better treatment of such infants (13). Finally, according to our experiences, and experiences from literature (5, 6, 8, 22), the best results can be achieved if we combine both aEEG and standard EEG. Some newer aEEG monitors have already incorporated both techniques in one machine (e. g. NicoletOne, Brainz) and even allow the option of recording multiple EEG channels for better seizure detection. In those instances where, according to aEEG result, one is not sure that a seizure has occured, concomitant EEG tracing can clearly confirm such a fact (figures 7 - 7a and 7b, figure 8). This new generation of aEEG machines may allow better seizure detection

in suspected cases and may increase our ability to detect seizure activity in high-risk neonates and in those infants where controversies exist regarding possible subtle seizures or some other paroxysmal (non-convulsive) events. The near future will confirm whether it is really important to treat as soon as possible not only clinically recognizable seizures, but also the subtle ones, with subclinical symptomatology, and we may also hope that such new guidelines will also enable new pharmacotherapies for sick newborns in this field.

CONCLUSION

Early and reliable determination of prognosis in neonates with acute encephalopathy is extremely important for all persons that care for such newborns and may in favourable cases reduce the anxiety of parents at an early stage. On the other hand today we are aware that early recognition of clinical (and most probably also subtle) seizures is a must because it will ensure early management as it has been proven that such a regime may substantially decrease future epilepsy. Both standard (digitalized and coupled with video) and amplitude integrated EEGs have already demonstrated their high capacities to predict neurological outcome and postneonatal epilepsy in infants with hypoxic-ischaemic encephalopathy. Awareness that both techniques have also some shortcomings has prompted new generation of recorders that display simultaneously aEEG and raw EEG and we believe that this will further increase our management possibilities for severely ill newborns treated at NICUs.

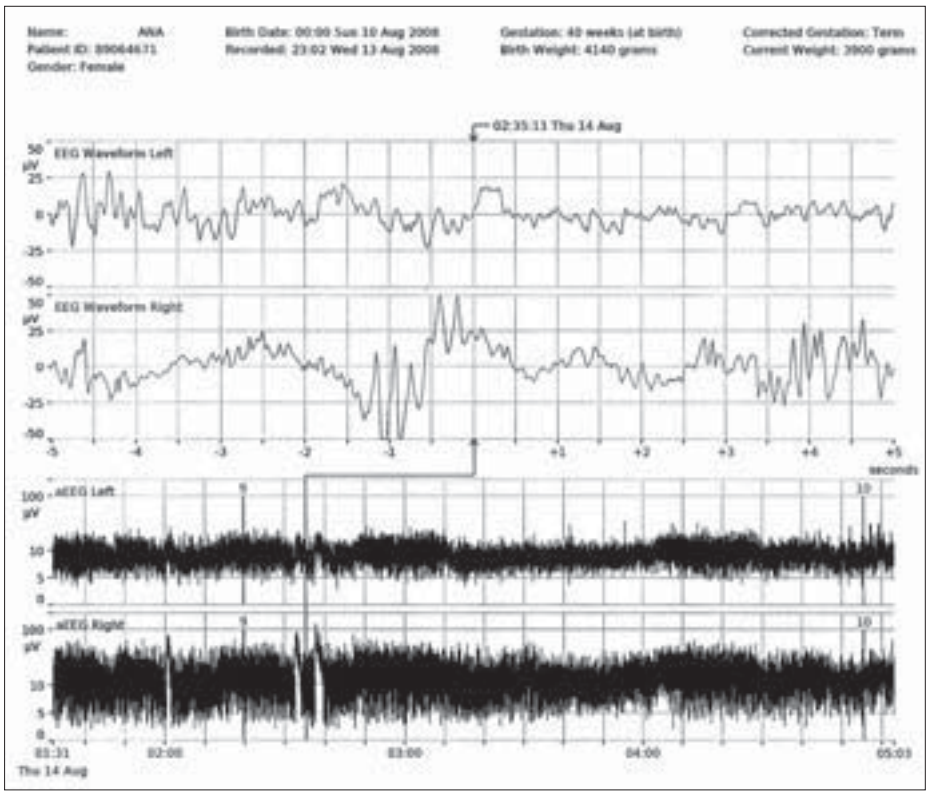

Figure 8. *Silent seizures recorded by aEEG (seen as white incisures in black background activity) and concomitant raw EEG signal confirming spiky graphoelements.*
Slika 8. *Električki napadaji zabilježeni na aEEG-u (vidljivi kao bijeli zarezi – usjekline u osnovnoj aktivnosti crne boje) i povremeni neodređeni EEG signal koji sadrži oštre grafoelemente.*

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DIJAGNOSTIČKE MOGUĆNOSTI VIDEO-ELEKTROENCEFALOGRAFIJE
I AMPLITUDNO-INTEGRIRANE ELEKTROENCEFALOGRAFIJE U RANOJ DJEČJOJ DOBI

D. Neubauer, D. Osredkar, D. Paro-Panjan, M. Derganc

Glavni ciljevi tijekom nadzora bolesne novorođenčadi su sprječavanje ili bar umanjivanje oštećenje mozga te postizanje optimalnog neurorazvojnog ishoda. Elektroencefalografiju, kao odraz električne aktivnosti mozga, smatramo najpouzdanijom metodom u prepoznavanju moguće disfunkcije središnjeg živčanog sustava (tj. konvulzija) kao i u predviđanju ishoda. Najbolje praćenje novorođenčadi i male djece možemo postići služeći se kontinuiranim funkcionalnim monitoringom, ali dugotrajni EEG ima ograničenu dostupnost u mnogim centrima i zahtijeva interpretaciju iskusnog pedijatra-elekroencefalografista. Tako je amplitudno integrirana EEG (aEEG) tehnika za pojednostavljeni EEG monitoring s rastućim kliničkim potencijalom u neonatalnoj intenzivnoj njezi. Ovaj rad prikazuje literaturne navode i podatke iz našeg osobnog iskustva s dijagnostičkim mogućnostima obje metode, standardnim (digitalnim, uz video) EEG-om, kao i aEEG-om te upućuje na važnost upotrebe aparata nove generacije koje na ekranu, uz aEEG signal, prikazuju i standardni EEG za uspješnije otkrivanje konvulzija.

Descriptors: ELECTROENCEPHALOGRAPHY – methods; VIDEO RECORDING; INTENSIVE CARE, NEONATAL – methods; SEIZURES – diagnosis; BRAIN DISEASES – diagnosis; HYPOXIA-ISCHEMIA, BRAIN - diagnosis

Primljeno/Received: 20. 10. 2008.
Prihvaćeno/Accepted: 17. 11. 2008.