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The field of clinical neurophysiology has expanded with the development of new approaches, techniques, and studies over the last two decades. In many cases, new neurophysiologic procedures and interpretations have allowed more accurate diagnosis, aided in diagnosis, and set the gold standard for diagnostic confirmation in numerous neurological disorders. Thus, clinical neurophysiology has grown and increasingly gained respect due to its diagnostic acumen. With this growth has come a wide diversity of subspecialty skills. Each subspecialty lends itself to focused research and, in many cases, clinical certification. In this regard, neurophysiologists skilled in sleep studies, for example, would find themselves unlikely to spend much of their time evaluating complex electromyography (EMG) cases. Pediatric or adult training creates another layer of differentiation so that the interpretation of an electroencephalogram (EEG) in an infant or child differs greatly from that of an adult. A lack of information focused on pediatric clinical neurophysiology exists, with most texts written largely with the adult patient in mind. This book uniquely bridges that gap by providing information from a pediatric perspective in various aspects of clinical neurophysiology. Contributors to this book are thought leaders and researchers in their respective fields of clinical neurophysiology. Each has provided discussion in their subspecialty area with a pediatric focus emphasizing diagnostic neurophysiologic techniques. Each chapter emphasizes a different focused area of neurophysiology and brings together the clinical and technical information needed for understanding. Chapters are devoted to pediatric sleep disorders, epilepsy, febrile seizures, and nonepileptic paroxysmal disorders. Other chapters are devoted to pediatric muscular dystrophies, EMG, brachial plexopathies, and peripheral neuropathy. A chapter devoted to intraoperative monitoring is included along with other chapters on evoked potentials and autonomic disorders. In several chapters, multiple authors have contributed, each providing aspects related to their research or area of unique expertise.

This book will serve as an excellent reference for the clinical provider as well as for trainees and technologists in gaining greater knowledge in the various subspecialty areas of clinical neurophysiology.
I want to thank the contributors of this book who, through their passion for the field of clinical neurophysiology, devoted much time to writing and sharing their wealth of information. Additionally, none of the research or clinical data would be possible without the patients who entrusted their care to us. Of course, the time devoted to research and dedication to the field of clinical neurophysiology would not be possible without the encouragement of mentors and the support of our families. My parents’ encouragement has been invaluable throughout my life. I dedicate this book to them and to my sons Nadeem and Corey who taught me how deep love can be. Never stop following your dreams, my darlings.

Gloria M. Galloway, MD, FAAN
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EEG Monitoring in Neonatal Epilepsies

Lekha M. Rao, MD
Joyce H. Matsumoto, MD
Jason T. Lerner, MD
Marc R. Nuwer, MD, PhD

Electroencephalographers often approach neonatal studies with trepidation. Neonatal studies vary from traditional electroencephalograms (EEGs) in both technical and visual aspects. Half of the full electrode set is used, placed at double distance, and the recording lasts for 60 minutes in order to catch a full sleep-wake cycle. Extra electrodes are also essential for interpreting the recording, such as ocular leads, chin electromyogram (EMG), and cardiac and respiratory monitoring. When interpreting the neonatal EEG, the paper speed is slowed to 15 mm/sec in order to more easily recognize the slower delta frequencies, which dominate in neonatal records. The low-frequency filter is set to 0.5 Hz in order to clearly interpret slow eye movements (1). Sensitivity is often lowered below the standard 7 mv/sec, given that amplitudes are not as high and scalp impedance is lower. Although these differences exist, with experience and knowledge of these EEG differences, interpretation in this age group is readily accomplished.

Much of the trepidation associated with the interpretation of neonatal EEG stems from the fact that “normal” background is somewhat of a moving target. Findings that are acceptable at 30 weeks conceptional age (CA) are grossly abnormal at 36 weeks. Therefore, neonatal EEG is best interpreted by first noting the infant’s current CA and then recognizing the characteristics that should be present in the EEG background of a normal neonate. CA is calculated by adding the estimated gestational age at birth to the current chronologic age (in weeks). If not given the correct gestational age, an age range can be estimated based on recognized patterns.
NEONATAL EEG BACKGROUND

Neonatal EEG studies should be systematically evaluated, with interpretation phrased in terms of several key features:

- Continuity
- Amplitude
- Symmetry
- Interhemispheric synchrony
- Normal named patterns

In extreme prematurity, normal electrographic findings are typically discontinuous, with bursts of continuous cerebral activity separated by intervals of relative quiescence and lower amplitude. This discontinuity improves with age, with the interburst interval becoming progressively shorter and higher in amplitude as the baby approaches full term. By 40 to 44 weeks CA, the EEG background becomes continuous in both wake and sleep (2).

Differentiation between wake and sleep states initially appears around 30 weeks CA. By definition, the infant is awake whenever his/her eyes are open and asleep when eyes are closed. Sleep is further subdivided into active sleep (AS, characterized by irregular respirations, occasional limb movements, and rapid horizontal eye movements) and quiet sleep (QS), characterized by deep, regular respirations and paucity of limb/trunk movement. Electrographically, wakefulness and AS in infants more than 30 weeks CA demonstrate fairly continuous cerebral activity, developing into a characteristic mixed frequency, moderate-amplitude activité moyenne pattern.

Because neonatal background abnormalities may become most apparent during deeper sleep stages, a complete assessment of the EEG background requires thorough evaluation of QS. To this end, continuous EEG (cEEG) provides a significant advantage over routine EEG in ensuring that a generous sample of QS is captured for review. As the invariant, nonreactive pattern of burst suppression seen in extremely preterm infants transitions into more defined wake-sleep stages around 30 weeks CA, the final remnants of EEG discontinuity linger in QS. As development proceeds, QS discontinuity gradually resolves, with gradual improvement in the duration and amplitude of the interburst activity. Between 30 and 32 weeks CA, QS activity consists of a tracé discontinue pattern in which periods of cerebral activity are separated by nearly isoelectric periods of quiescence with voltage less than 25 μV. With time, the voltage of the interburst intervals gradually increases such that by 35 to 36 weeks CA, QS typically transitions to a tracé alternant pattern, in which cerebral activity is consistently maintained above 25 μV but cycles between higher-amplitude bursts and more quiescent periods. The interburst amplitude continues to increase until no periods of relative quiescence are perceived, and a continuous slow-wave sleep pattern is fully established around 44 weeks CA (3,4).

Bursts of activity appearing in one hemisphere within 1.5 seconds of the other hemisphere are considered to be synchronous. Prior to 30 weeks CA, cerebral activity occurs nearly...
simultaneously in both the right and left hemispheres, a phenomenon described as a hypersynchrony \( (5) \). The reason for early interhemispheric hypersynchrony is unknown, though it has been postulated to be related to prominent thalamic drivers without significant cortical input. Following 30 weeks, occasional asynchronous bursts are seen, which progressively diminish until 100% synchrony is reestablished around 37 weeks CA.

**BACKGROUND PATTERNS**

A. Excessive sharps

B. Excessive discontinuity

C. Brief ictal/interictal rhythmic/repetitive discharges (BIRDs)

D. Other patterns (depressed/undifferentiated, low voltage)

EEG background findings (Table 1.1) are also frequently employed to assess the functional integrity of the neonatal brain and to aid in the evaluation of neurologic prognosis. At the same time, however, many patterns are nonspecific and of uncertain clinical significance.

**TABLE 1.1 EEG Background in Prematurity**

<table>
<thead>
<tr>
<th>CONCEPTIONAL AGE (WEEKS)</th>
<th>MAXIMUM INTERBURST DURATION (SEC)</th>
<th>EEG BACKGROUND FEATURES</th>
</tr>
</thead>
<tbody>
<tr>
<td>24–25</td>
<td>60</td>
<td>No sleep organization or reactivity</td>
</tr>
<tr>
<td>27–30</td>
<td>35</td>
<td>Discontinuous in both wake and sleep, some reactivity</td>
</tr>
<tr>
<td>31–33</td>
<td>20</td>
<td>Differentiation between active and quiet sleep patterns</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wake and active sleep: mixed frequency continuous ( (activité moyenne) )</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Quiet sleep: interburst intervals amplitude nearly isoelectric, (&lt;25 , \mu V) (trace discontinue pattern)</td>
</tr>
<tr>
<td>34–36</td>
<td>10</td>
<td>Wake and active sleep: mixed frequency continuous ( (activité moyenne) )</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Quiet sleep: Interburst intervals increase in amplitude, eventually exceeding 25 ( \mu V ) (trace alternant pattern)</td>
</tr>
<tr>
<td>37–40</td>
<td>6</td>
<td>Wake and active sleep: mixed frequency continuous ( (activité moyenne) )</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Quiet sleep: Interburst intervals continue to increase in amplitude, increasing continuity (trace alternant) transitioning to continuous slow-wave sleep pattern</td>
</tr>
</tbody>
</table>

Source: Adapted from Refs. 5, 8, 9.
Excessive Sharps

Temporal sharp transients are normally seen during sleep in the term neonate, are often bilateral and asynchronous, and should be surface negative in polarity. If they occur in runs, are unilateral, or appear in wakefulness, they are more likely to be considered abnormal. Sharp waves occurring outside of the temporal or centrotemporal regions would also be considered abnormal. No official criteria exist in which temporal sharps are defined as excessive, and it has been proposed that greater than 13 over the course of a 60-minute recording in a term neonate would be considered excessive [criteria adapted from (6,7)].

Excessive Discontinuity

In the term neonate, periods of attenuation during QS should not exceed 2 to 4 seconds in duration. Interburst intervals longer than this are considered excessively discontinuous. This pattern can be associated with dysmaturity or incorrect gestational dating but can also be a nonspecific marker for neonatal encephalopathy.

Brief Ictal/Interictal Rhythmic/Repetitive Discharges

First described by Shewmon in 1990, this pattern is considered interictal but on the ictal spectrum. It usually occurs in the context of electrographic seizures and is characterized by a run of epileptiform discharges with evolution but lasting less than 10 seconds. Their clinical significance is not yet completely understood, but given their presence in neonates with seizures, they may be associated with neurologic morbidity.

Depressed/Undifferentiated or Low Voltage

A depressed and undifferentiated pattern (Figure 1.1) is most commonly associated with severe underlying neurologic injury to the cortical generators of electrocerebral activity. Low voltage is considered to be background activity persistently less than 10 μV without normal background features. The recording will also show poor reactivity, no alteration in frequencies with external stimulation, and no sleep-wake cycling.

SEIZURE DETECTION

Seizure is the most common neurologic disorder in the neonatal period. There are numerous potential etiologies for neonatal seizures, and timing of presentation as well as electrographic findings can be of potential use in elucidating their etiology. Seizures can be transient due to an acute injury, markers of an underlying genetic or metabolic disorder, or signs of an underlying structural abnormality.

EEG evaluation and confirmation of seizure activity is particularly important in the neonatal population, given the high rate of subclinical or subtly clinical seizures and because newborns may often have unusual movements that can be mistaken for seizure activity. For instance, a systematic video review of 526 electrographic seizures in nine infants revealed that only 34% of seizures were associated with clinical manifestations, and only 27% of these clinical seizures
(9% of overall seizures) were recognized by nursing staff. Of more concern, 73% of “seizures” documented by the neonatal intensive care unit (NICU) nursing staff were not epileptic seizures. Rather, the events marked by NICU nursing were not epileptic in nature. Instead, these movements commonly consisted of likely nonepileptic events such as jitteriness, mouthing, and fisting (10). Therefore neonatal seizure quantification solely by clinical observation is plagued by both high false-positive and high false-negative rates. To ensure an accurate assessment of seizure detection and treatment response, EEG monitoring is essential.

Subclinical Seizures

EEG confirmation of seizure cessation following anticonvulsant treatment is also recommended. Neonates are particularly vulnerable to the phenomenon of electroclinical uncoupling, in which clinical evidence of seizure activity ceases, following the administration of seizure medications, while subclinical electrographic seizure activity continues unabated. Although subclinical seizures are known to occur in critically ill children and adults (11,12), features of chloride homeostasis unique to the immature brain contribute to a high likelihood of electroclinical uncoupling. The potassium-chloride cotransporter (KCC2), which is the predominant type of chloride channel in the adult brain, transport chloride ions outside of neurons and have a hyperpolarizing effect. In contrast, the predominant chloride channel in the immature brain is the sodium-potassium-chloride cotransporter (NKCC1),
which transports chloride ions into neurons and has a depolarizing effect. Gamma aminobutyric acid (GABA), a neurotransmitter that activates chloride channels, can therefore have a paradoxically excitatory effect in developing neurons due to the predominance of NKCC1 channels (13). Because the transition from NKCC1 to KCC2 chloride channels occurs in a caudal-to-rostral progression, GABA initially becomes inhibitory in subcortical structures such as the brainstem and basal ganglia while remaining excitatory in the cortex. Commonly used medications such as phenobarbital, which exert their effects through GABA agonist activity, may therefore suppress brainstem motor output, while allowing electrographic seizure activity to continue in the cortex.

The high risk of subclinical seizures has been well documented in the NICU population (14–17). For instance, cEEG monitoring of neonates randomized to initial treatment with either phenobarbital or phenytoin demonstrated that while 24 of 50 infants responded completely to the first seizure medication administered, 15 of the remaining 26 neonates (58%) demonstrated electroclinical uncoupling, with suppression of clinical seizure activity during all or the majority of posttreatment electrographic seizures (18).

**Neonatal Seizure Semiology**

Seizure semiology in the newborn is variable but can be grouped into the following categories: clonic, tonic, and myoclonic (Table 1.2). These are focal, repetitive, and cannot be suppressed by the examiner. Due to incomplete myelination, infants cannot generate generalized tonic-clonic seizures, but they can have multifocal seizures that can appear generalized to the untrained or inexperienced examiner. Infants can also have generalized epileptic spasms that are hypothesized to be more subcortically driven.

Because infants often have repetitive movements which can be difficult to interpret, EEG is often relied upon to distinguish stereotyped or rhythmic movements as epileptic or nonepileptic. Oral automatisms, bicycling, roving eye movements, and other nonrhythmic but repetitive movements are often seen in critically ill infants. Without clear electrographic correlate, these had been previously termed *clinical only* seizures, but are now more commonly presumed to be

<table>
<thead>
<tr>
<th>MOVEMENT TYPE</th>
<th>LOCALIZATION/CLINICAL</th>
<th>ELECTROGRAPHIC CORRELATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonic</td>
<td>Focal rhythmic jerking of an extremity</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Nonsuppressible</td>
<td></td>
</tr>
<tr>
<td>Tonic</td>
<td>Focal sustained extension or flexion of an extremity</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Not able to overcome with external manipulation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sustained extension of the whole body</td>
<td>Not usually</td>
</tr>
<tr>
<td>Myoclonic</td>
<td>Single jerk or multiple nonrhythmic jerks of an extremity</td>
<td>Usually</td>
</tr>
<tr>
<td>Spasms</td>
<td>Focal or generalized</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Flexor, extensor, or mixed flexor-extensor</td>
<td></td>
</tr>
</tbody>
</table>

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nonepileptic in nature. These movements tend to occur more often in encephalopathic infants and are also associated with poor prognosis (19).

**Role of Amplitude-Integrated EEG**

The use of amplitude-integrated EEG (aiEEG) is now growing in the NICU, because it offers an opportunity for continuous monitoring of cerebral activity in a manner that can be interpreted at the bedside by the neonatologist rather than requiring a certified electroencephalographer. With the growing use of therapeuthic hypothermia for hypoxic-ischemic encephalopathy (HIE) in the NICU, aiEEG has become more widely used concurrently in monitoring for seizures and change in background activity.

aiEEG differs from conventional EEG in that it involves the use of only four electrodes and relies on the trending of voltage and comparison between the two hemispheres. The timescale is also broader, with the evaluation of 8 to 12 hours of data on one screen, as opposed to 20 to 30 seconds per screen of a conventional EEG.

Background activity on conventional EEG can be assessed using continuity, amplitude, and symmetry, all of which can also be assessed on aiEEG in a different manner. Interburst interval cannot be precisely interpreted with this method, but voltage over time is averaged in order to give a range of activity, which can then be interpreted. This is tightly linked to amplitude, where the peak-to-peak interval of minimum and maximum voltage ranges is represented as bandwidth. If the minimum voltages are consistently less than 5 μV and maximum less than 10 μV, this is considered a low-voltage, suppressed background. Normal activity is considered to be a minimum voltage of greater than 5 μV and maximum voltage greater than 10 μV.

Seizures are detected on aiEEG as a relative increase in overall amplitude over a given period of time. These can be detected by relative increases of the peak-to-peak amplitude with narrow bandwidth. Some indication of localization can be inferred if this occurs only in one hemisphere. Overall seizure burden can also be inferred, based on the number of peaks of increased voltage peaks. (20)

However, a limitation of condensing this data and relying on voltage alone is that aiEEG can be ripe with artifact. When the baby is handled and high-amplitude electrode artifact is generated, this will appear as an amplitude spike on aiEEG. Similarly, when continuous external artifacts such as EKG rhythm occur in the setting of a low-voltage, suppressed background, this can be misrepresented as a normal voltage range on aiEEG.

aiEEG has been shown in studies to be sensitive, but not very specific for the identification of an abnormal background and seizures (21). Regardless, given the ease of use, the widespread availability, and the ability for bedside interpretation, aiEEG has now become part of the standard of care during therapeutic hypothermia for HIE of the newborn (22–24). Studies have shown that the use of aiEEG may even be beneficial in that neonates are being treated for seizures only with electrographic confirmation, rather than purely on a clinical basis (25).

**TRANSIENT OR “BENIGN” NEONATAL SEIZURES**

**Hypoxic-Ischemic Encephalopathy**

HIE is the leading cause of seizures in the neonatal period, with an incidence of 2 to 5 per 1,000 live births. Seizures have been found in up to 80% of this population, but this may be an
underestimation, given that continuous EEG monitoring is not routinely used. aiEEG is often used in the NICU to fulfill the need for continuous electrographic monitoring.

Therapeutic hypothermia has also become the standard of care in the treatment of infants with HIE and has been shown to improve neurodevelopmental background. Evaluation of background activity can be useful for prognostication in infants with HIE. Persistently abnormal background activity without evidence of improvement over time is more likely to be associated with a worse neurodevelopmental outcome. A normal background or improvement in background is less likely to be associated with poor neurodevelopmental outcome.

Recent studies have shown a high incidence of seizures in infants undergoing therapeutic hypothermia for HIE, up to 40% to 60%, with 35% to 75% of these being subclinical (26,27) (Figure 1.2). The burden of seizures is highest in the first 24 to 48 hours, with a natural decline after 72 hours (28). It is presumed that a higher burden of seizures is associated with worse neurodevelopmental outcome; however, this is a topic of much debate, as infants with more severe HIE are also likely to have more refractory seizures. Additionally despite advances in antiepileptic drug development, relatively few advances have been made in the treatment of seizures due to HIE, and many treatments also have potential unwanted side effects in the developing brain (29,30).

Benign Familial Neonatal Convulsions

Benign familial neonatal convulsions are often seen around the fifth day of life, giving them the frequently used descriptive term of “fifth day fits.” Most are associated with a mutation in the KCNQ2 gene coding for a voltage-gated potassium channel, which has autosomal transmission, but other potassium channels as well as the sodium channel, such as SCN2A mutation, have also been implicated (31). There is often a family history of neonatal seizures, and the electrographic background is frequently normal but can show excessive discontinuity and excessive sharp transients. These were initially termed benign because there was thought to be no long-term consequence, although recent studies have shown that this is not always the case. KCNQ2 mutations have also been associated with Ohtahara syndrome, and the phenotype can be variable, with seizures persisting well beyond the neonatal period (32,33).

Stroke

Perinatal stroke is also a common cause of neurologic morbidity in the newborn period. The majority are arterial ischemic, although at least 30% can be venous in nature (34). Seizures are a common presentation of neonatal arterial ischemic stroke; up to 72% present with seizures (35). In a neonate with persistently unilateral seizures, arterial ischemic stroke should be strongly considered as an etiology and neuroimaging should be undertaken.

Hypoglycemia and Other Reversible Causes

Neonatal hypoglycemia is a frequent complication of infants of mothers with gestational diabetes, but can also be seen in well neonates with poor feeding. The occipital lobes are particularly at risk because of the high metabolic demand of the visual cortex. Persistent focal seizures can be seen emanating from either posterior quadrant. Imaging can show diffusion restriction in the areas affected, partly due to frequent seizures and increased local metabolism and partly due to watershed ischemia. These areas can later undergo laminar necrosis and develop the appearance of ulegyria.
FIGURE 1.2 A 41+1-week-old baby boy with hypoxic-ischemic encephalopathy and meconium aspiration syndrome on selective hypothermia therapy, with seizures starting on the first day of life. This recording shows a seizure starting at T4.
Other electrolyte and metabolic disturbances can also precipitate seizures in the neonatal period, similar to adults. Hypomagnesemia, hypocalcemia, hyponatremia, and hyperbilirubinemia can also lead to neonatal seizures. In these instances, correction of the underlying etiology is necessary to effectively treat the seizures (34).

CATASTROPHIC EPILEPTIC ENCEPHALOPATHIES

There are several conditions presenting in the neonatal period which have been termed “catastrophic,” in that they are associated with frequent seizures and severe interictal background abnormalities which, without prompt remedy, almost inevitably result in poor neurodevelopmental outcome (Table 1.3).

Ohtahara Syndrome

Ohtahara syndrome, also known as early infantile epileptic encephalopathy with suppression-burst presents in early infancy. Initial symptoms are seen within the first 3 months, frequently within the first 2 weeks. Clinically this presents with brief (less than 10 seconds) tonic spasms (generalized or focal), which occur independently or in clusters. Other seizure types including focal seizures, hemiconvulsions, or tonic-clonic seizures are seen in approximately 33%. Most cases are related to a variety of structural brain lesions, although metabolic and genetic disorders have been reported. Mutations associated include syntaxin binding protein 1 (STXBP1), Aristaless-related homeobox (ARX), sodium channel SCN2A, and KCNQ2 (36–39).

The typical EEG pattern is a consistent (wake and sleep) “suppression-burst” pattern with periods of diffuse amplitude suppression alternating with bursts of high amplitude spike and polyspike discharges.

Diagnosis of Ohtahara syndrome is based on the clinical picture and EEG findings. The prognosis is poor, with many affected children dying in infancy. Survivors have developmental impairment and many have chronic seizures or evolve into Lennox-Gastaut or West syndrome. Anti-seizure medications are used; however, there is no specific evidence-based therapy known. Surgery has been performed for cases with clear focal lesions (40).

<table>
<thead>
<tr>
<th>TABLE 1.3 Neonatal Epilepsy Syndromes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EPILEPSY SYNDROME</strong></td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td>Ohtahara syndrome</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Early myoclonic epilepsy of infancy</td>
</tr>
<tr>
<td>Malignant migrating partial seizures of infancy</td>
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Early Myoclonic Epilepsy of Infancy

Early myoclonic epilepsy of infancy (EMEI) was described shortly after Ohtahara syndrome and there are a number of similarities between them. EMEI also begins within the first 3 years, although it can present as early as a few hours after birth. Clinically this begins with focal myoclonus that can shift between different body parts often in an asynchronous and random pattern. A wide range of focal seizures (anything from tonic posturing to autonomic signs) is very common and tonic spasms are also seen. There is a range of underlying disorders associated with EMEI including structural lesions and metabolic and genetic abnormalities. In contrast to Ohtahara syndrome, diffuse cortical atrophy, rather than focal structural lesions, is typically seen. A variety of metabolic abnormalities have been associated, in particular, non-ketotic hyperglycinemia (41). Mutation of the v-erb-a erythroblastic leukemia viral oncogene homologue 4 (ErbB4), which is associated with cortical migration, is also related (42).

The typical EEG pattern of EMEI is similar to the suppression-burst pattern seen in Ohtahara syndrome; however, in EMEI the suppression-burst pattern is not continuous and occurs more prominently (or exclusively) in sleep. The myoclonic seizures are not generally associated with changes on the EEG.

EMEI is also diagnosed clinically and treated with antiseizure medications. Additionally treatment of the underlying metabolic disorder may be helpful. The prognosis of EMEI is also very poor, with 50% of patients dying by 3 years and the survivors having severe developmental impairment (40).

Malignant Migrating Partial Seizures of Infancy

Malignant migrating partial seizures of infancy (MMPSIs) present in the first 6 months of life with multifocal, bilateral, independent seizures. Seizures are very difficult to control and are associated with progressive developmental impairment and a decrease in the head circumference. The underlying etiology is unknown; however, it is likely genetic. Mutations have been found in a number of genes including SCN1A, phospholipase C beta 1 (PLCB1), KCNT1, and TBC1D24.

The ictal EEG shows focal seizures initiating from different locations in both hemispheres that “migrate” from one area to another (Figure 1.3).

MMPSI is diagnosed by clinical presentation along with the typical EEG pattern and has a poor prognosis. Status epilepticus is common and may be related to patients dying in the first 2 years of life (43).

OTHER EPILEPSY SYNDROMES PRESENTING IN NEONATES

Hemimegalencephaly (HME) is a severe developmental brain anomaly characterized by the overgrowth of one hemisphere. This is associated with epilepsy, psychomotor retardation, and contralateral motor defect. Seizure types include focal motor seizures, asymmetric tonic or clonic seizures, and epileptic spasms. HME is one of the causes of Ohtahara syndrome (Figure 1.4) and West syndrome and is associated with a variety of genetic abnormalities and neurocutaneous syndromes; however, it may be an isolated syndrome.
Patients with West syndrome associated with HME may have a unique EEG background called hemihypsarrhythmia (high amplitude, poorly organized with multifocal spikes over the affected side only) (Figure 1.4).

(text continues on page 16)
FIGURE 1.3 (continued) (B) Seizures arose from all electrodes, often with a new seizure emerging amidst the existing seizure at a noncontiguous electrode. This demonstrates seizures occurring independently at C3 and C4, as evidenced by nonsynchronous frequencies. (continued)
FIGURE 1.3 (continued)
FIGURE 1.4 (A) A 38+6-week-old baby boy with left-body focal motor seizures starting day of life 1, found to have right hemimegalencephaly. This background in wakefulness demonstrates epileptiform discharges over the right hemisphere. (B) In sleep, the background is discontinuous with excessive discontinuity more prominent over the right hemisphere. (continued)
Diagnosis of HME is based on imaging including asymmetry of the hemispheres and ventricles, loss of gray-white differentiation, neuronal heterotopia, thick cortex, and abnormalities in the gyri, basal ganglia, and internal capsule. The clinical course and prognosis is dependent on seizure control, the severity of the affected side, the ability of the contralateral side to compensate, and early surgery (44).
METABOLIC EPILEPSIES

Pyridoxine-dependent epilepsy was first described by Hunt and colleagues in 1954. This syndrome is unique in that it is severe but treatable, and thus early recognition is of tantamount importance. This syndrome has an estimated birth incidence between 1:400,000 and 1:750,000. Seizures can be prenatal in onset and can include multiple seizure types, including infantile spasms and focal, multifocal myoclonic, and tonic seizures. There can also be an associated encephalopathy, which may manifest as tremulousness, irritability, or hypothermia. The baseline EEG will show a continuous spike-wave or burst-suppression pattern. Diagnosis is established by giving an intravenous dose of 100-mg pyridoxine during EEG monitoring, which will often lead to the resolution of epileptiform activity and improvement of the background (Figure 1.5). The response is often seen rapidly, although delayed responses have also been reported. Relapses can occur after a median of 9 days if pyridoxine therapy is withheld, and therefore patients need to remain on lifelong therapy (45).

Folinic acid–responsive seizures are another treatable cause of neonatal seizures. EEG background features and seizure types can be similar to pyridoxine-dependent seizures, and concurrent pyridoxine dependency can occur within individuals. Seizures respond to 2.5- to 5-mg folinic acid given twice daily, and daily doses should be added for patients with an incomplete response to pyridoxine treatment.
FIGURE 1.5 (A) A 40+5–week-old baby boy who presented with “jitteriness” and episodes of flexor spasms 3 hours after birth. Initial background was discontinuous and asynchronous. (B) After pyridoxine administration, the background normalized, becoming synchronous and continuous.

REFERENCES


