

Advancing Neurologic Care in the Intensive Care Nursery

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AUTHOR DISCLOSURE

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Educational Gaps

1. Avoiding hyperthermia and maintaining normal glucose, carbon dioxide and oxygen, and blood pressure can help to minimize brain injury.
2. Clinical observation of seizures is not reliable.

Abstract

Up to 25% of neonates at tertiary care nurseries are diagnosed as having neurologic conditions, including encephalopathy and hypoxic-ischemic encephalopathy [HIE], as well as seizures, stroke, and intracranial hemorrhage. These children are at high risk for lifelong disabilities, including cerebral palsy, epilepsy, and cognitive and behavioral disabilities. Establishing a neurointensive care nursery involves a culture change toward brain-focused care, with all bedside clinicians (including physicians, nurses, respiratory technologists, and trainees) maintaining constant awareness of the potential neurologic complications of critical illnesses, as well as the effect of management on the developing or injured brain. Team-based, brain-focused care to monitor, diagnose, and treat neurologic conditions of the developing brain has the potential to improve outcomes in neonates with brain injuries and congenital conditions of the developing nervous system.

Objectives

After completing this article, readers should be able to:

1. Explain the benefits of brain-focused care.
2. Identify clinical, neurophysiologic, and radiographic signs of encephalopathy and brain injury.
3. Incorporate brain-focused care into daily clinical practice.

Introduction

Neonates with critical illnesses are now surviving after hospitalization thanks to advances in resuscitation and cardiopulmonary support. However, the risk of neurologic injuries and lifelong disabilities remains unchanged. Neurologic conditions in the neonatal intensive care unit (NICU) are common; up to 25% of children at tertiary care hospitals are diagnosed as having neurologic conditions, including encephalopathy and HIE, as well as seizures, stroke, and intracranial hemorrhage. (1)(2)

Brain-focused care for neonates evolved from the adult neurocritical care model, where a coordinated approach by the bedside improves outcomes, through the following:

1. Early recognition and treatment of neurologic conditions;
2. Prevention of secondary brain injury through attention to basic physiologic factors (temperature regulation, glucose homeostasis, oxygenation, and blood pressure support);
3. Consistent management using guidelines and protocols; and
4. Use of experienced specialized teams at dedicated referral centers. (3)

The neonatal neurocritical team includes a neonatologist, a neurologist, and a specialized bedside nurse. Other team members may include a neurosurgeon, epileptologist, and developmental care specialist. (4)

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Identifying Encephalopathy and Brain Injury

Neurocritical care involves brain-focused care, that is, constant awareness by all team members of the state of the developing brain in response to injury, critical illness, medications, and medical procedures. Three main methods are used to assess brain function and structure: clinical examination, neurophysiologic monitoring, and imaging.

Neurologic Examination

The neurologic examination remains the primary means of identifying neonates with suspected conditions of the nervous system. Neonatologists must become adept at neurologic examination and localization of clinical findings. Describing the neurologic examination as *nonfocal* is inadequate (newborns with large hemispheric strokes or hemorrhages can have symmetrical examinations, and so this term has little meaning in the neonatal context). Mental status examination starts with observation of spontaneous actions; neonates with decreased responsiveness are stimulated with increasingly noxious stimuli (voice, light, touch, and pain), and the response is noted. Does the neonate cry? Does he/she open his/her eyes? Does he/she move? A clinical observation that a neonate has few spontaneous movements but opens eyes and has complex movements to central pain is more informative than saying that he/she is “lethargic.” Cranial nerve testing includes observation of pupillary response, grimace, and suck in all neonates and oculocephalic maneuver (doll’s eyes), corneal reflex, and gag in an unresponsive neonate. The motor examination includes examination of muscle bulk, tone (resistance to passive movement), and power. Low tone and weakness can be difficult to tell apart—a neonate with low tone but normal power will generate full resistance to a painful stimulus but have excess and easy range of motion in response to passive movements. Tendon reflexes help to localize a lesion to the peripheral nervous system when depressed. Numerous primitive reflexes have been described; the most important reflexes to be tested on each examination include Moro reflex, grasps, and suck. An intubated infant can undergo a complete neurologic examination with some caution. Sedatives, such as opiates and benzodiazepines, may decrease responsiveness but should not make the neonate unresponsive if the neuraxis is intact, unless used in high doses or the child is preterm.

Neonatologists must be especially adept at identifying neonates who qualify for therapeutic hypothermia. Recent California Perinatal Quality Care Collaborative (CPQCC) recommendations are that all neonates born at 35 weeks’ gestation and age 6 hours or younger who

have one or more of the following undergo additional blood gas analyses, examination for signs of encephalopathy, and observation for seizures: Apgar score of 6 or less at 10 minutes, history of acute perinatal event, continued positive pressure ventilation or cardiopulmonary resuscitation at 10 minutes, or cord blood gas pH of 7 or less or base excess of -10 or less. (5) Not all neonates with these broad parameters will qualify for cooling; however, the careful monitoring recommended by the CPQCC should increase the number of eligible neonates who are identified. All neonates with one or more of these signs should have temperature monitored to prevent hyperthermia and undergo serial examinations to look for signs of encephalopathy during the first 6 hours after birth. Signs of moderate or severe encephalopathy include decreased or absent spontaneous movements; decreased or absent response to touch, sound, light, and pain; abnormal posture or tone; abnormal cranial nerve reflexes (including pupillary and oculomotor response and gag); decreased or absent primitive reflexes (suck or Moro reflex); and seizures. Some neonates who are irritable or hyperalert may progress to develop seizures and decreased responsiveness, and so some centers are cooling these neonates on a case-by-case basis.

Brain Monitoring and Seizure Detection

Brain monitoring using full or adapted montage electroencephalography (EEG) (**Figure**) is necessary to assess background brain function in critically ill neonates with encephalopathy, brain injury, or suspected seizures. (6) Video-EEG is the gold standard for seizure diagnosis. Adapted montage and trending, such as amplitude-integrated EEG (aEEG), are useful for detecting some seizures. (7) Bedside brain monitoring, such as aEEG, can be applied by the bedside nurse shortly after admission and interpreted with minimal training, and it provides nurses, physicians, and trainees at the bedside with an opportunity to directly observe brain function on an hour-to-hour basis to assess for seizures, response to medications, and response and recovery to injury. Both EEG and aEEG can be applied and run simultaneously on the same machine. (7) Each neonatal neurocritical care bed should be wired to transmit monitoring data for remote access and interpretation by a neurophysiologist.

Neonates with neurologic conditions often have paroxysmal spells that are concerning for seizure and seizures are often the first sign of a serious underlying condition. Unfortunately, clinical observation of a spell is usually insufficient to determine whether it will have an electrographic correlate. In one study, more than 100 bedside

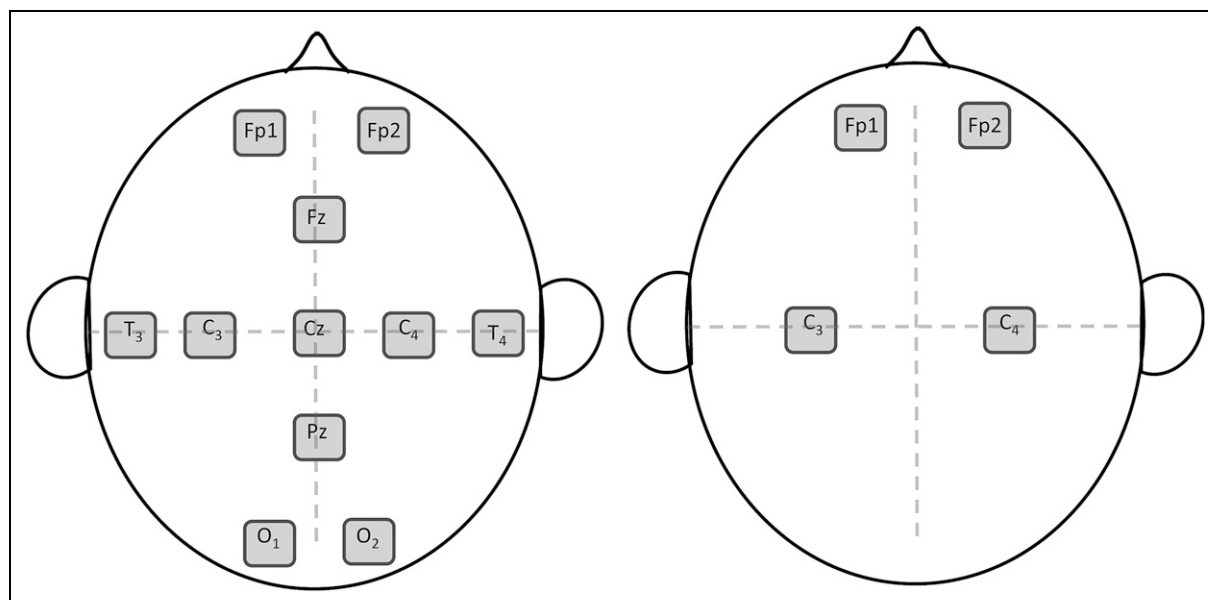


Figure. Left. The international 10–20 system for electroencephalographic (EEG) electrode placement, modified for neonates, includes the electrode positions indicated by the boxes. Right. One example of an adapted montage that uses standard 10–20 placement. Three amplitude-integrated EEG channels are formed: Fp₁–C₃, Fp₂–C₄, and C₃–C₄.

clinicians were shown seizure and nonseizure videos; correct identification rate was, on average, 50%. (8) Only seizures detected by EEG need to be treated; therefore, brain monitoring is essential to guide appropriate medical management. There are 2 specific scenarios in which the semiology of the event can guide the initial management. First, bilateral, rhythmic jerking of upper and/or lower extremities of an otherwise well neonate during sleep (with events that terminate when the child is aroused) likely represents benign neonatal sleep myoclonus, and seizure medication is not warranted. Second, hemiclonic motor seizures in an otherwise well child starting in the first 2 days after birth likely represent stroke, and seizures should be treated promptly and monitoring initiated without delay. After medication administration, many neonates have electroclinical dissociation (ie, continuation of seizures identified on EEG without clinical correlate). Subclinical seizures are also very common in critically ill neonates with encephalopathy (and subclinical status epilepticus is present at the onset of EEG recording in approximately 5% of patients with HIE). (9)

Most seizures in neonates are due to acute symptomatic causes (eg, HIE, stroke, hemorrhage, and hypoglycemia). Rarely, seizures are due to genetic causes (eg, benign familial neonatal epilepsy or neonatal onset epileptic encephalopathy due to KCNQ2/3 mutations in neuronal voltage-gated potassium channels), inborn errors of metabolism, or brain malformations. Acute

management of seizures includes emergency investigation of treatable causes (eg, hypoglycemia, hypocalcemia, and infection), rapid initiation or review of monitoring, and rapid treatment (Table 1). Seizure guidelines that outline first-, second-, and third-line treatments and are endorsed by neurology, neonatology, and nursing leaders can help improve the speed of medication administration.

Both EEG and aEEG are also useful to help determine prognosis. For neonates who receive therapeutic hypothermia, a normal early aEEG or EEG is associated with a good outcome, whereas a persistently abnormal aEEG or EEG background at 24 to 48 hours is highly predictive of adverse neurodevelopmental outcome. (10)(11)(12)

Brain monitoring should continue for at least 24 hours in patients at high risk for seizures, for 24 hours after the last electrographic seizure, or for long enough to capture 2 to 4 clinical events when the indication is to assess paroxysmal events that are suspicious for seizure. (6)

Optical Near-Infrared Spectroscopy

Near-infrared spectroscopy (NIRS) is a noninvasive method for trending of brain tissue oxygenation. Tissue oxygenation index and regional cerebral oxygen saturation are measurements that reflect the saturation of oxygen in veins (70%–80%), capillaries (5%), and arteries (20%–25%). NIRS appears useful to guide hemodynamic

Table 1. **Emergency Management of Suspected or Confirmed Seizures**

Bedside glucose measurement
 Measurement of electrolytes, including calcium
 Sepsis and meningitis evaluation as clinically indicated
 Initiate monitoring (preferably with continuous video-EEG)
 Consult a neurologist
 Treat with phenobarbital, 20 mg/kg, for confirmed EEG seizures or suspected seizures in high-risk conditions (eg, HIE with suppressed EEG in the first 48 hours, suspected stroke)
 Review EEG periodically to assess for seizures without clinical correlate
 Treat recurrent acute symptomatic EEG seizures with additional medications (eg, phenobarbital up to 40–50 mg/kg; fosphenytoin up to 30 mg/kg and/or levetiracetam up to 60 mg/kg). Medications should be tailored based on the clinical condition, institutional availability, and clinical diagnosis.
 MRI brain with DWI and MRS
 For acute symptomatic seizures (ie, HIE, stroke, hemorrhage, or hypoglycemia), consider discontinuing medications once seizures have resolved for 24–72 hours
 For seizures that persist beyond 72–96 hours, consider underlying epilepsy or epileptic encephalopathy as the cause.

DWI=diffusion weighted imaging; EEG=electroencephalography; HIE=hypoxic-ischemic encephalopathy; MRI=magnetic resonance imaging; MRS=magnetic resonance spectroscopy.

management to optimize cerebral oxygenation in preterm neonates. (13) Its role in establishing prognosis in term neonates with HIE is uncertain, although it is unlikely to be superior to EEG and magnetic resonance imaging (MRI). (14)(15)

Brain Imaging

Bedside head ultrasonography and MRI are the most important modalities for imaging the neonatal brain. Computed tomography should be avoided because it exposes the neonate to radiation. Neurosurgical conditions, such as intracranial hemorrhage and hydrocephalus, can be well imaged by serial head ultrasonography; assessment of tissue injury is best made by MRI and can usually wait until MRI is available.

MRI should be performed for all neonates with a suspected neurologic condition. Magnetic resonance sequences must be adapted for the high water content of the neonatal brain. Routine neonatal sequences include conventional T1 and T2-weighted MRI, which is important for detailing anatomy; diffusion weighted imaging to reveal areas of injury within the last 7 to 10 days; susceptibility weighted imaging to reveal areas of hemorrhage; and magnetic resonance spectroscopy to assess brain metabolites. Magnetic resonance angiogram and venography are useful to detail congenital vascular malformation (eg, vein of Galen malformation) and to assess for clot in the setting of focal injury or intraventricular hemorrhage in a term neonate. Fluid attenuated inversion recovery sequences are less useful given the high water content of the neonatal brain. MRI is prognostic

for developmental disabilities in both preterm and term neonates. (16)(17)(18)

Preventing Secondary Injury and Protecting the Newborn Brain

Preventing secondary injury is a primary focus of neonatal neurocritical care. Brain-focused care begins in the delivery room. Preterm very low-birth-weight (<1,500 g) neonates are at high risk for brain injury because of the physiologic immaturity of the cardiopulmonary and cerebral autoregulatory systems, as well as fragility of the germinal matrix. In term neonates who are born after fetal distress, end-organ failure can lead to inadequate brain perfusion or hypoglycemia and subsequent secondary injury after an initial peripartum insult. Measures to resuscitate and stabilize cardiopulmonary function must also take into account the developing and injured brain. After performing resuscitation according to the Neonatal Resuscitation Program guidelines, clinicians should maintain physiologic homeostasis of all organ systems to help prevent secondary brain injury (Table 2).

Therapeutic hypothermia is the only proven therapy for protecting the term newborn brain. It is safe and effective for reducing death and disability at 18 to 22 months when initiated within 6 hours after birth in neonates with encephalopathy due to suspected or confirmed HIE. (19) The benefits of hypothermia extend into childhood, with lower rates of cerebral palsy and low IQ and higher rates of normal outcome among school-aged children who underwent hypothermia. (20) Therapeutic hypothermia should be applied as soon as possible

because outcomes are improved with earlier onset of cooling. (21)(22)(23) Frequent core temperature monitoring is necessary to prevent the temperature from decreasing rapidly below 33.0°C. Servo-regulated cooling devices for medical transport are now available, can reduce the time to achieving therapeutic temperature, and can prevent temperature fluctuations and severe hypothermia. (24)

Providing therapeutic hypothermia in the setting of a specialized neurocritical care service may offer the following benefits:

1. Rapid initiation of hypothermia by an experienced team;
2. Continuous monitoring and rapid treatment of seizures 24 hours per day, 7 days per week;
3. MRI sequenced and interpreted by specialists; and
4. Counseling for parents by experienced physicians and nurses.

Neonates who are undergoing therapeutic hypothermia should be monitored with continuous, prolonged EEG or aEEG. Although hypothermia may reduce the rate of seizures among neonates with moderate encephalopathy, the risk remains approximately 50%. (9)(25) (26) The risk for seizures is highest (approximately 60%) among neonates whose EEG background is abnormal at the onset of recording; however, even neonates with a normal EEG have an approximately 10% risk of electrographic seizures. (9)

MRI is important for determining the presence and degree of brain injury among neonates who undergo hypothermia. It is also useful for detecting other causes of encephalopathy or abnormal neurologic examination

findings, such as brain malformation or inborn error of metabolism. The best timing for MRI will depend on the experience and resources of the center. Imaging just after therapeutic hypothermia has ended (ie, days 4–6) offers the following advantages: (1) lower need for sedation to achieve good quality images because many remain encephalopathic, and (2) the MRI can serve as a good turning point between the acute phase of the admission and recovery and planning for home. MRI on days 10 to 14 is preferred at some centers. There are rare reports of evolution of brain injury that is apparent only on a later scan, and the patient may be more clinically stable at this time point. Patients who undergo imaging early and have normal MRI results but persistent abnormal neurologic examination or EEG results and/or difficulty establishing feeding should undergo MRI again in the second week of age.

Not all neonates who undergo hypothermia will escape adverse outcome. The rate of death or disability was approximately 50% in the randomized clinical trials. (27) For this reason, there is an active push to develop adjunctive treatments to hypothermia, as well as novel agents that will be neuroprotective or neuroregenerative for other types of brain injury and also for neonates who are born preterm. Early preclinical and clinical investigations reveal promise for a number of agents, including erythropoietin, xenon, and melatonin. (28)(29)

Establishing a Neonatal Neurocritical Care Service

Establishing a neurocritical care or neonatal neurocritical care service involves a culture change toward

Table 2. Brain-Focused Care to Prevent Secondary Injury

Parameter	Strategy
Oxygenation and ventilation	Support pulmonary function as needed Avoid hyperoxia to minimize risk of oxidative stress (use room air when possible) Avoid hyperventilation and hypocapnia to minimize risk of disrupted cerebral autoregulation and reduced cerebral perfusion
Blood pressure support	Support normal hemodynamics for adequate brain perfusion through volume replacement with normal saline or blood Provide pressors as needed Avoid rapid shifts in blood pressure to minimize risk of intraventricular hemorrhage in preterm neonates
Temperature control	Hyperthermia can exacerbate underlying brain injury and lead to worse outcome in the setting of brain injury Maintain normothermia
Glucose management	Low plasma glucose can cause de novo brain injury or worsen existing tissue damage Carefully monitor and treat hypoglycemia

Table 3. The Neonatal Neurocritical Care Team

Clinician	Role	Common Role
Specialized bedside nurse	<ul style="list-style-type: none"> Completes rapid triage of patient and equipment Recognizes first signs of brain injury Applies specialized equipment (eg, cooling device and aEEG) 	<ul style="list-style-type: none"> Apply standardized guidelines Perform recurrent neurologic examinations Determine eligibility for neuroprotection and research studies Plan investigations Interpret aEEG Communicate with family – anticipate needs Determine diagnosis and prognosis
Neonatologist	<ul style="list-style-type: none"> Provides cardiopulmonary stabilization Corrects hypoxia/hyperoxia, hypocarbia, hypoglycemia, hyperthermia, and hypotension Applies advanced cardiopulmonary support (eg, blood pressure, ventilation, ECLS) 	
Neonatal neurologist	<ul style="list-style-type: none"> Investigates mechanism of injury and differential diagnosis Oversees application and interpretation of video-EEG Manages seizures Orders appropriate MRI sequences and provides interpretation Discusses prognosis with bedside team and family Provides long-term neurologic care, as needed 	

aEEG=amplitude-integrated EEG; ECLS=extracorporeal life support; EEG=electroencephalography; MRI=magnetic resonance imaging.

brain-focused care. The goal is for all bedside clinicians (including physicians, nurses, respiratory technologists, and trainees) to maintain constant awareness of the potential neurologic complications of critical illnesses, as well as the effect of management on the developing or injured brain. Most neurocritical care services are closed units with the neonatologist acting as the physician of record and the neurologist acting as a consultant with an early and active role in decision-making and communication with the family. Many units have trained specialized bedside nurses to provide neurologic care. The core members and roles of the neonatal neurocritical care team are outlined in Table 3. Establishing local guidelines that have been approved by senior NICU leadership, as well as leaders from neonatology, neurology, and nursing, can help to standardize care, improve the speed of administration of neuroprotective treatments, improve patient safety, and minimize errors. Examples of guidelines may include therapeutic hypothermia, seizure management, stroke management, and MRI transport. The neonatal neurocritical care unit may be a virtual

space, a specific area within the NICU, or a separate unit.

Conclusion

Neonatal neurocritical care (also called neurointensive or brain-focused care) is a subspecialty that developed in response to recent advances in brain care and improved understanding of the effect of critical illness on the developing brain. Technological advances, such as digital EEG with bedside trending and remote access availability, allow the bedside care clinicians to assess brain function in real time. Safe, high-resolution brain imaging techniques using magnetic resonance allow bedside physicians to assess the effect of critical illness on brain structure and development. Team-based, brain-focused care to monitor, diagnose, and treat neurologic conditions of the developing brain has the potential to improve outcomes in neonates with brain injuries and congenital conditions of the developing nervous system.

NOTE: The content of this article is solely the responsibility of the author and does not necessarily represent the official views of the National Institutes of Health.

American Board of Pediatrics Neonatal-Perinatal Content Specifications

- Know the indications for and limitations of various neurodiagnostic tests.
- Know the indications for and limitations of various neuroimaging studies and be able to recognize normal and abnormal structures and changes during development and growth.
- Know the management of perinatal asphyxia, including neural protective strategies.
- Understand the spectrum of clinical seizures in the newborn infant.
- Understand the differential diagnosis and evaluation of neonatal seizures.



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