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NON-CONVENTIONAL USE OF AMPLITUDE INTEGRATED ELECTROENCEPHALOGRAPHY (AEEG) - LESSONS FROM A TERTIARY NICU

By Patrick J McNamara, MD

Background

The ability to monitor global cerebral brain activity is increasingly being recognised as an essential component of neonatal intensive care. The traditional approach to neurological monitoring has involved periodic "snap-shot" clinical, conventional electroencephalography (EEG) or neuroimaging assessments which typically occur after the insult has occurred and thus limit early detection or prevention of neurological compromise. Amplitude integrated electroencephalography (aEEG) technology was initially developed in the late 1960s for adults suffering from neurological depression or injury or undergoing surgery using the first cerebral function monitor (CFM).[1] However, due to technical constraints and the need for constant recalibration, the technology was abandoned. The technology was reintroduced in the mid 1980s by neonatologists for assessing infants who had suffered a hypoxic-ischemic insult. Early studies using the CFM showed close correlation to conventional EEG.[2] Several studies have now demonstrated that early aEEG in the first 6 hours of life is a sensitive tool for predicting the severity of hypoxic-ischemic encephalopathy (HIE) and the potential consequences in full term infants.[3,4] The potential benefits of early aEEG monitoring has been further emphasized in the recent hypothermia trial by Gluckman et al where subgroup analysis demonstrated a benefit only in those patients with moderately abnormal background activity and not in those with severe trace abnormalities.[5] More recent studies of the evolution of aEEG background activity have shown that the recovery of aEEG background activity by 24 hours(6) and earlier return of sleep wake cycling (SWC)[7] help further refine the ability to predict a good outcome. Although the emphasis of aEEG monitoring has focused on asphyxiated infants, neonates with seizure disorders or those with intracranial pathology, the technology offers the potential of dynamic cerebral monitoring in critically ill neonates who are at risk of or may have suffered some form of neurological compromise.

Trends in aEEG Monitoring

Over the past 5 years the number of neonatal intensive care units (NICU) providing bedside aEEG has increased remarkably. Bedside aEEG satisfies many of the requirements of an ideal point of care device, namely its user-friendliness, the ease of interpretation, portability, immediate availability and reproducibility of the results. This has led to increased aEEG research and clinical usage in non-conventional disease processes or populations. aEEG has recently been shown to be feasible for monitoring cerebral activity in preterm infants and normative values have been established.[8] In

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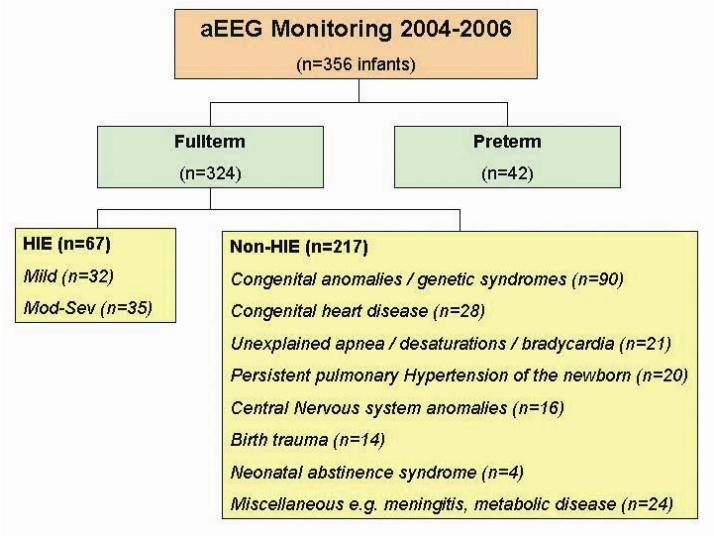

Figure 1. Profile of clinical scenarios where aEEG monitoring has been used for neurological surveillance at the Hospital for Sick Children, Toronto.

particular SWC can be clearly identified on the trace from around 30 weeks gestation although a cyclical pattern emerges in some babies at 25-26 weeks gestation. A scoring system has been proposed based on continuity, presence of cycling, amplitude of the lower border and bandwith. The effects of intraventricular hemorrhage[9,10], hypotension[10], hypoglycaemia[11], pneumothorax[12] and drugs including anticonvulsants[12-14] on characteristics of aEEG traces have also been studied.

Introduction of aEEG to a Tertiary NICU

Since July 2004 aEEG was introduced to the NICU at the Hospital for Sick Children, Toronto, Ontario, Canada close to 400 babies have been monitored with either the CFM (Olympic Medical ltd, Seattle, US) or BrainZ (BrainZ Ltd, Auckland, New Zealand) monitors. Of these, only 18% (67/356) of cases have been for neurological surveillance in classical HIE to guide therapeutic interventions or assist with neurological prognostication (Figure 1). The current guidelines used in our NICU (Table 1) suggest aEEG monitoring in neonates with acute or chronic neurological disease, medical problems where there may be co-existing development brain problems or clinical scenarios where illness acuity is high [e.g. cardiogenic shock, persistent pulmonary hypertension of the neonate (PPHN)] and the risk of secondary neurological injury is increased. The rationale is that critically ill neonates with CHD, PPHN, or extreme biochemical (e.g. hyponatraemia, hypernatraemia) & metabolic disturbance (e.g. hyperammonaemia, lactic acidosis) or sepsis are at increased risk of abnormal neurological events or adverse neurodevelopmental outcomes. Whether aEEG monitoring can influence these outcomes has yet to be determined, however in the patients we have monitored it has helped guide the extent of the neurological work-up and refine long-term follow up of these patients.

The following two cases are examples of scenarios where non-conventional use of aEEG was helpful in guiding intensive care management of the patients.

Case I

Summary: Full-term male infant with respiratory distress, circulatory compromise and features of encephalopathy admitted on day 4 of life.

A healthy full-term male infant, weighing 3.7 kg, was born at a local hospital to a G3P2 mother, after a normal antenatal course and delivery. A history of parental consanguinity was noted. The Apgar score was normal although some delay in onset of spontaneous respirations was noted at birth.

Postnatal Course: He was noted to be slightly tachypneic in the first few hours after birth. However, he was discharged after 24 hours. He fed well until day three when he became very irritable and fed poorly. He was taken to an emergency room where he was resuscitated with crystalloid (0.9% NaCL) and commenced on nasal continuous positive airway pressure (nCPAP).

Physical Assessment: On admission to our outborn tertiary NICU he was noted to be tachycardic (179/min), tachypneic (65/min), hypertensive (96/79 mmHg) with delayed capillary

Table 1. Current Medical Indications for aEEG Studies at the Hospital for Sick Children, Toronto

1. Hypoxic – Ischemic Encephalopathy
2. Seizures or clinical scenario mimicking seizure disorders (e.g., apnea, hypertension, tachycardia)
3. Significant neurological disorders (e.g., congenital brain malformations, vascular lesions)
4. Post cardiac arrest
5. Inborn error of metabolism (e.g., urea cycle disorders, hypoglycemia, hypocalcemia)
6. Neonatal abstinence syndrome (e.g., alcohol/opiate withdrawal)

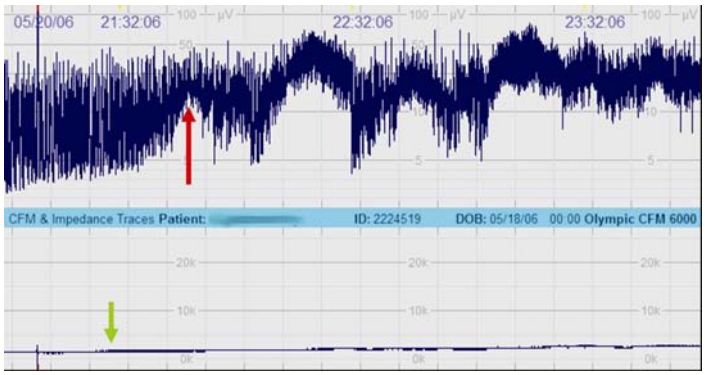

Figure 2. aEEG trace showing background activity (top) and impedance (bottom) during suspected seizure activity. The cerebral background activity demonstrates a moderately abnormal pattern (lower margin < 5) with no sleep wake cycling initially (before the red arrow). At 21:50 there is a sudden and sustained rise in both the lower and upper margin of the trace. This rise is commonly seen during periods of seizure activity. It is important to point out that the impedance is low (< 10k) throughout the period of recording so interpretation of the trace should be reliable.

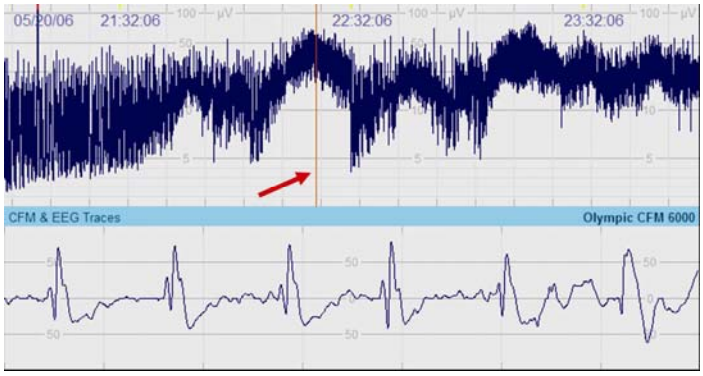

Figure 3. aEEG trace showing background activity (top) and raw EEG trace (bottom) during suspected seizure activity. The newer aEEG monitors allow real-time visualization of the raw EEG which assists the medical team with confirmation of seizure-like episodes. In this trace when the raw EEG is analyzed during the suspected period of seizure activity (red arrow) a rhythmic "spike and wave" type pattern is demonstrated (bottom trace). The pattern oftentimes resembles a cardiac dysrrhythmmia.

refill (4-5 seconds). His oxygen saturation was 99% in room air. He was lethargic and there was little spontaneous movement. Neurological examination revealed distal hypertonia, hyperreflexia and ankle clonus. The urine was noted to be unusually turbid and abnormal in colour.

Impression: The clinical impression was felt to be consistent with a diagnosis of sepsis with possible meningitis. An inborn error of metabolism and duct-dependent left ventricular outflow tract lesion were also considered as alternative diagnoses.

Investigations: The initial plasma hematocrit was 73 % and a partial exchange transfusion was performed. Blood was sent for plasma lactate, ammonia and metabolic screen. Two-dimensional echocardiography revealed a structurally normal heart with suboptimal biventricular performance. aEEG monitoring was commenced as a result of ongoing encephalopathy and persistent hypertension (systolic blood pressure > 100 mmHg). The initial background activity was consistent with a moderately abnormal pattern (Figure 2), however after 30 minutes of monitoring a marked elevation (red arrow) in the lower margin occured. This was not due to movement artifact as the impedance (green arrow) remained at a low level throughout. Further evaluation of the raw EEG confirmed the elevations in the lower margin to be prolonged episodes of seizure activity (Figure 3) although there were no obvious clinical seizures apart from systemic hypertension and altered sensorium. The overall interpretation of this trace is consistent with non-convulsive status epilepticus.

Management: He was intubated and mechanically ventilated due to the cardiorespiratory instability, presence of seizures and potential likelihood of further deterioration. Intravenous milrinone was commenced for myocardial dysfunction and low cardiac output state. He received a bolus of phenobarbitone which resulted in cessation of the seizure activity on aEEG (Figure 4, red arrow) and normalization of his blood pressure. Plasma lactate was 4.4 mmol/l and ammonia was 632 mmol/l. Further metabolic testing confirmed a diagnosis of Arginosuccinic aciduria which is a Urea Cycle disorder with a very poor prognosis.

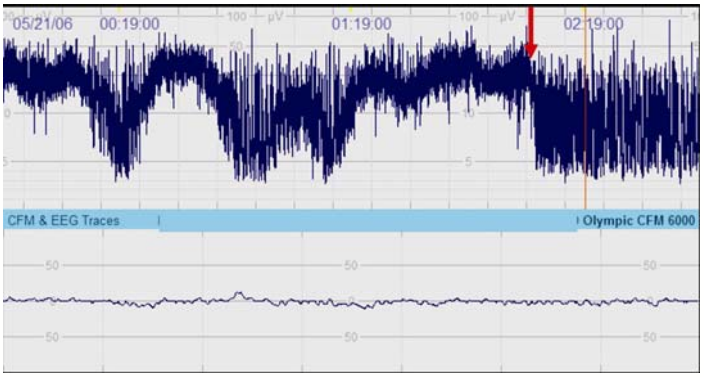

Figure 4. aEEG trace showing background activity (top) and raw EEG trace (bottom) after anti-convulsant therapy. After the administration of phenobarbitone (red arrow) the cerebral background activity returns to its pre-seizure status (moderately abnormal pattern). The raw EEG no longer demonstrates the rhythmic "spike and wave" type pattern.

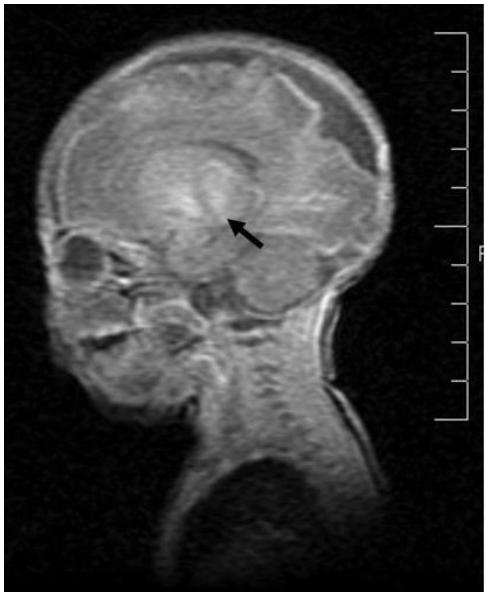

Figure 5. MRI scan of the brain taken on day 6 of life. The image presented is a sagittal view of the right side of the brain which demonstrates increased signal in the thalamus and caudate nucleus on diffusion weighted imaging (black arrow). The left side of the brain showed similar changes.

This case emphasizes the importance of dynamic monitoring of cerebral activity in critically ill neonates with subtle features of encephalopathy. The only clues to the presence of seizure activity were the altered sensorium and systemic hypertension. The ability to perform aEEG monitoring resulted in the confirmation of seizure activity and the commencement of anticonvulsant therapy. Whilst standard EEG remains the gold standard for seizure detection oftentimes it can be difficult to obtain an urgent EEG, particularly outside of normal working hours at nights and weekends. In these situations aEEG may be a useful tool to screen for seizure activity, however, a standard EEG should be performed as a follow up in these patients as aEEG may not detect brief or focal seizures in some patients.[15]

Case II

Summary: Premature infant with atypical seizures after an acute neurological insult.

Birth History: A premature infant was born at 30 weeks gestational age to a primigravida mother after spontaneous onset of preterm labour secondary to placental abruption. The Apgar scores were 0, 2 and 4 at one, five and ten minutes respectively, and she required aggressive resuscitation.

Postnatal Course: In the first 24 hours of life she developed profound hypoglycaemia (plasma glucose 0.9 mmol/l) and systemic hypotension (mean arterial pressure 20 mmHg) requiring therapeutic intervention. She was treated for clinical seizures on day 2 of life. Her initial neurological examination showed generalized hypotonia, paucity of spontaneous movements, absent gag reflex and limited papillary responsiveness. The ultrasound scan of brain on day two of life was reported as normal and over the first week of life her neurological status deteriorated somewhat. A Magnetic Resonance Imaging (MRI) scan of brain was performed on day 6 of life which dem-

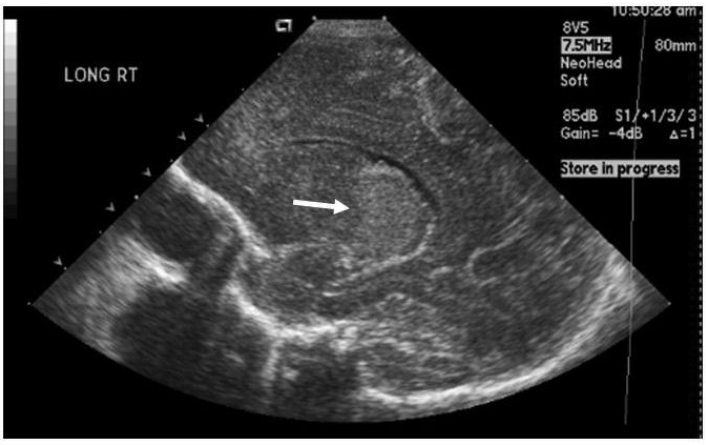

Figure 6. Ultrasound scan of brain performed on day 11 of life. The image presented demonstrates increased echogenicity of the right thalamic nucleus (white arrow). The left side of the brain showed similar changes.

onstrated hypoxic-ischemic injury in the basal ganglia (Figure 5). A repeat cranial ultrasound on day 11 also demonstrated diffuse increased echogenicity in the basal ganglia (Figure 6). The conventional EEG on day 5 was reported as mildly abnormal and visual evoked potentials performed at the same type were noted to be absent.

On day 35 of life she started to develop profound episodes of oxygen desaturation to < 65% that were associated with profound apnea. She was aggressively treated for gastro-esophageal reflux with multiple agents, but the episodes persisted. She was also transitioned to continuous enteral feeds through a gastrostomy tube, but again, without major effect. The EEG was repeated on day 45 to screen for seizure activity, but was reported as normal. By day 53 (38 weeks corrected gestation) her neurological examination was significantly abnormal with generalized hypertonia, hyper-reflexia and ankle clonus consisted with early spastic quadraplegia. The absent gag reflex persisted and she had no suck response. aEEG monitoring was commenced on day 53 to investigate dynamically over a longer period of time the possible relationship between the apnea/desaturation episodes and seizure activity. The aEEG demonstrated moderately abnormal background activity and multiple episodes of seizure activity which coincided with the apneic episodes (Figure 7). She was treated with phenobarbitone and the spells improved significantly.

This case emphasizes the merits of aEEG in screening for seizure activity in patients where acute changes in cardiovascular or respiratory physiology can't otherwise be explained. It must acknowledged that aEEG is less sensitive than standard EEG for seizure detection. However, in scenarios where the one episode or "parachute EEG" assessment does not coincide with clinical deterioration, abnormal seizure activity may be missed. Continuous video-EEG is not readily available in most NICUs but aEEG offers the advantage of continuity and timely information which may be related to the clinical deterioration.

aEEG and Neonates with Acute Cardiovascular Compromise

Continuous monitoring of heart rate, respiratory rate, oxygen saturations and intermittent monitoring of blood pressure and body temperature are standard practices in the NICU. Acute changes in these parameters may reflect either normal physiologic variation or a pathologic disease process that may warrant therapeutic intervention. It is known that critically ill neonates with acute cardiovascular compromise due to CHD or PPHN are at increased risk of abnormal neurodevelopmental outcome; however, continuous neurological monitoring in these "at risk" populations is usually not performed. Neonates with duct-dependent pulmonary (e.g. transposition of the great arteries) or systemic (e.g. hypoplastic left heart syndrome) lesions are at increased risk of acute hypoxaemia or low cardiac output state respectively, to an extent that compromised cerebral metabolism may lead to cell death. The risk of an adverse neurological event is significantly increased in neonates with CHD requiring cardiopulmonary bypass or postoperative extracorporeal life support (ECLS).[16] Recent MRI studies have identified cerebral white matter abnor-

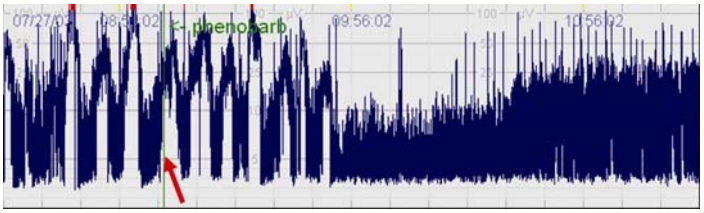

Figure 7. aEEG trace showing moderately abnormal background activity (lower margin < 5) with frequent episodes of sudden elevation of the lower and upper margins consistent with seizure activity. The impedance was normal throughout. The administration of phenobarbitone (red arrow) led to termination of these episodes however the moderately abnormal background persisted.

malities preoperatively in at least 50% of full term neonates.[17] There is a strong correlation between these findings and preoperative arterial PaO_2 and blood pressure. The preterm neonate with CHD is theoretically even more vulnerable due to the effects of chronic hypoxemia and intermittent periods of systemic hypoperfusion on the developing brain. PPHN is a failure of postnatal cardiopulmonary adaptation due to persistent elevation in pulmonary vascular resistance. Oftentimes, these babies are profoundly hypoxemic and require aggressive cardiotropic support for hemodynamic instability. Although short and long-term outcomes have improved somewhat over the past 10 years, it remains an important cause of neonatal morbidity and mortality. Survivors have an increased risk of neurodevelopmental and audiological impairment (46%), cognitive delays (30%), hearing loss (19%) and risk

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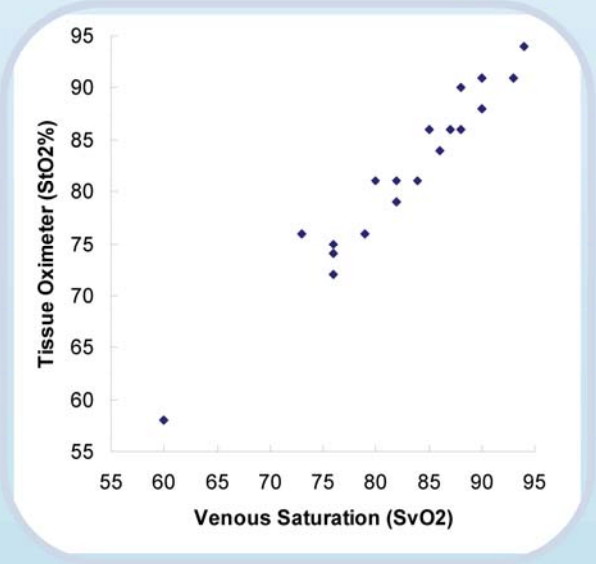

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of rehospitalization (22%).[18] An improved understanding of the relationship between tissue oxygenation or organ perfusion and dynamic measures of cerebral performance may facilitate earlier detection of "at risk" scenarios which may be conducive to interventions. A recent study of aEEG monitoring in neonates with CHD requiring post-operative ECLS demonstrated abnormal background activity in 53% of neonates.[19] Although background activity improved by discharge, in some patients a severely abnormal aEEG trace predicted death or intracranial neuropathology with a sensitivity of 1.0 (0.85-1.0) and specificity of 0.75 (0.52-0.75). In a small review of 30 non-asphyxiated neonates admitted to our NICU with a diagnosis of PPHN or CHD, an abnormal aEEG trace was identified in 50% cases (unpublished data). The long term significance of this finding remains unknown. However, in patients with abnormal aEEG where MRI of brain was performed (n=5) all but one had abnormal findings that are known to be associated with poor neurodevelopmental outcome. aEEG may certainly, at least, guide selection of patients for more detailed neuroimaging and neurodevelopmental follow-up. There are some pitfalls to aEEG monitoring in neonates with respiratory failure, particularly those on high-frequency modes of ventilation. The vibration from high-frequency oscillator or jet ventilators may be transmitted to the head region, resulting in motion artifact and trace alteration. In these patients it is important to survey the impedance trace concurrently with the background activity as this will show the degree of ventilator artifact. Nevertheless, the role of aEEG monitoring and the implications of an abnormal trace in this population is worthy of prospective evaluation.

Guidelines for Integration of the Technology

All health care professionals (i.e. physicians, nurses, respiratory therapists and nurse practitioners) involved in the care of critically ill newborn infants should have an active participant role in aEEG monitoring. These roles must be clearly defined to ensure this technology is used correctly and analyzed in a timely fashion, thus ensuring optimal care is provided. Early identification of disturbances in global cerebral brain wave activity may lead to earlier therapeutic interventions, ultimately improving patient outcomes. It is important to designate an individual(s) who will take leadership for ensuring effective and safe use of the technology. They will assume responsibility for ensuring staff education, troubleshooting equipment-related issues and developing a clinical infrastructure within the NICU to govern aEEG usage. The latter should include the development of a reporting system to ensure accurate documentation of trace interpretation in the patient's chart and a system for long-term data storage. These traces may prove to be excellent resources for educational activities and may also facilitate clinical research.

Conclusions

aEEG monitoring is now available in many neonatal intensive care units and is most commonly used for monitoring neonates with established brain injury due to hypoxic-ischemic encephalopathy or seizure disorders. The increased availability of bedside

tools such as aEEG which provide a dynamic assessment of cerebral electrical activity offers the opportunity of prospectively evaluating the effects of hypoxemia, hypotension, low cardiac output states and interventions for them on global cerebral performance. This fertile area of research may help bridge current gaps in our understanding of heart-brain interactions and lead to earlier identification and more focused treatment of "at-risk" patients.

Addendum: Consent has been obtained from the families of the patients presented for dissemination of the clinical material.

I would like to acknowledge Dr. Jonathan Hellman for his constructive comments and feedback.

References

1. Maynard D, Prior PF, Scott DF. Device for continuous monitoring of cerebral activity in resuscitated patients. Br Med J 1969; 4:545-6.

2. Viniker DA, Maynard DE, Scott DF. Cerebral function monitor studies in neonates. Clin Electroencephalogr 1984; 15:185-92.

3. al Naqeeb N, Edwards AD, Cowan FM, Azzopardi D. Assessment of neonatal encephalopathy by amplitude-integrated electroencephalography. Pediatrics 1999; 103:1263-71.

4. Toet MC, Hellstrom-Westas L, Groenendaal F, Eken P, de Vries LS. Amplitude integrated EEG 3 and 6 hours after birth in full term neonates with hypoxic-ischaemic encephalopathy. Arch Dis Child Fetal Neonatal Ed 1999; 81:F19-F23.

5. Gluckman PD, Wyatt JS, Azzopardi D, Ballard R, Edwards AD, Ferriero DM et al. Selective head cooling with mild systemic hypothermia after neonatal encephalopathy: multicentre randomised trial. Lancet 2005; 365:663-70.

6. ter Horst HJ, Sommer C, Bergman KA, Fock JM, van Weerden TW, Bos AF. Prognostic significance of amplitude-integrated EEG during the first 72 hours after birth in severely asphyxiated neonates. Pediatr Res 2004; 55:1026-33.

7. Osredkar D, Toet MC, van Rooij LG, van Huffelen AC, Groenendaal F, de Vries LS. Sleep-wake cycling on amplitude-integrated electroencephalography in term newborns with hypoxic-ischemic encephalopathy. Pediatrics 2005; 115:327-32.

8. Burdjalov VF, Baumgart S, Spitzer AR. Cerebral function monitoring: a new scoring system for the evaluation of brain maturation in neonates. Pediatrics 2003; 112:855-61.

9. Hellstrom-Westas L, Klette H, Thorngren-Jerneck K, Rosen I. Early prediction of outcome with aEEG in preterm infants with large intraventricular hemorrhages. Neuropediatrics 2001; 32:319-24.

10. Greisen G, Pryds O, Rosen I, Lou H. Poor reversibility of EEG abnormality in hypotensive, preterm neonates. Acta Paediatr Scand 1988; 77:785-90.

11. Pryds O, Greisen G, Friis-Hansen B. Compensatory increase of CBF in preterm infants during hypoglycaemia. Acta Paediatr Scand 1988; 77:632-7.

12. Hellstrom-Westas L, Rosen I, Svenningsen NW. Cerebral complications detected by EEG-monitoring during neonatal intensive care. Acta Paediatr Scand Suppl 1989; 360:83-6.

13. ter Horst HJ, Brouwer OF, Bos AF. Burst suppression on amplitude-integrated electroencephalogram may be induced by midazolam: a report on three cases. Acta Paediatr 2004; 93:559-63.

14. van Leuven K, Groenendaal F, Toet MC, Schobben AF, Bos SA, de Vries LS et al. Midazolam and amplitude-integrated EEG in asphyxiated full-term neonates. Acta Paediatr 2004; 93: 1221-7.

15. Rennie JM, Chorley G, Boylan GB, Pressler R, Nguyen Y, Hooper R. Non-expert use of the cerebral function monitor for neonatal seizure detection. Arch Dis Child Fetal Neonatal Ed 2004; 89:F37-F40.

16. Dittrich H, Buhrer C, Grimmer I, Dittrich S, Abdul-Khaliq H, Lange PE. Neurodevelopment at 1 year of age in infants with congenital heart disease. Heart 2003; 89:436-41.

17. Galli KK, Zimmerman RA, Jarvik GP, Wernovsky G, Kuypers MK, Clancy RR et al. Periventricular leukomalacia is common after neonatal cardiac surgery. J Thorac Cardiovasc Surg 2004; 127:692-704.

18. Lipkin PH, Davidson D, Spivak L, Straube R, Rhines J, Chang CT. Neurodevelopmental and medical outcomes of persistent pulmonary hypertension in term newborns treated with nitric oxide. J Pediatr 2002; 140:306-10.

19. Pappas A, Shankaran S, Stockmann PT, Bara R. Changes in amplitude-integrated electroencephalography in neonates treated with extracorporeal membrane oxygenation: a pilot study. J Pediatr 2006; 148:125-7.

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Medical Products, News and Information

Phototherapy for Neonatal Jaundice Associated with Increased Risk of Skin Moles in Childhood

Children who received light therapy (phototherapy) for jaundice as infants appear to have an increased risk of developing skin moles in childhood, according to a report in the December issue of Archives of Dermatology, one of the JAMA/Archives journals. Some types of moles are risk factors for developing the skin cancer melanoma.

Jaundice or hyperbilirubinemia occurs when bilirubin, a yellow pigment created as a byproduct of the normal breakdown of red blood cells, cannot yet be processed by a newborn's liver and builds up in the blood, turning the skin, whites of the eyes and mucous membranes yellow. The condition affects between 45% and 60% of healthy babies and as many as 80 percent of infants born prematurely, according to background information in the article. During phototherapy, the treatment of choice for jaundice, babies are placed under blue lights (bili lights) that convert the bilirubin into compounds that can be eliminated from the body. Studies have been performed to assess the safety of this therapy, but many have not focused on its effects on the skin, the authors write.

Emmanuelle Matichard, MD, Bichat-Claude Bernard Hospital, Saint-Antoine Hospital, Assistance Publique-Hôpitaux de Paris, and colleagues assessed the presence of melanocytic nevi (moles) in 58 French children who were 8 or 9 years old at the time of the study. Eighteen children had phototherapy as newborns; 40 who were the same age but did not have phototherapy were recruited from a public school and served as controls. All the children and their parents were interviewed about the use of phototherapy, history of sun exposure and sunscreen use. A dermatologist performed physical examinations on the children and recorded their skin color, eye color, hair color, skin type and the number and size of moles.

Thirty-seven children (63%) had moles that were 2 millimeters or larger, and there was an average of 2.09 moles per child. Those who were exposed to phototherapy had significantly more moles of this size than those who did not-an average of 3.5 vs. 1.45 per child. When the analysis was limited to moles between 2 millimeters and 5 millimeters, the association was stronger. "Lentigo simplex [moles smaller than 2 millimeters in diameter] may represent more recent nevi, whereas those nevi due to early events should be larger," the authors write. "Nevi larger than 5 millimeters probably are congenital nevi and are most probably associated with genetic predisposition." These associations did not change when other risk factors for the frequency of moles, including skin type and light hair, were considered. Sun exposure, particularly during vacations, was also associated with the number of moles of all sizes, and light hair color was correlated with the number of moles smaller than 2 millimeters.

The study did not examine whether phototherapy increases the risk for melanoma in adults, and it is possible that the small difference in the number of moles between the two groups would not change their risk of developing cancer. However, further study could help illuminate the association. "Higher numbers of acquired benign nevi are associated with increased risk of melanoma," they conclude. "A detailed evaluation of the factors responsible for the development of nevi in children would be useful to identify high-risk groups to be targeted for prevention. The link between melanoma and phototherapy should be the focus of such a study."

Treatment Discovered for Deadly Childhood Disease

Researchers have discovered that a treatment involving enzyme replacement therapy dramatically reduces the risk of death in children with Pompe disease, a rare genetic disorder in which most children die before their first birthday. The disorder causes profound muscle weakness and heart and breathing problems and affects as many as one in 40,000 births. The study is published in the online edition of Neurology, the scientific journal of the American Academy of Neurology.

“This form of treatment has changed the natural history of this otherwise lethal disease,” said study author Priya Sunil Kishnani, MD, with Duke University in Durham, North Carolina.

The year long study involved 18 children under the age of six months with rapidly progressing Pompe disease. Pompe disease is caused by a deficiency in the enzyme acid a-glucosidase (GAA), which is needed to break down glycogen, a complex sugar molecule which releases glucose.

The study found all 18 children who started to receive the enzyme replacement, recombinant human GAA (rhGAA), before they were six months old survived to at least 18 months of age. Fifteen of the 18 children also did not need a ventilator. The study showed that starting rhGAA before the age of six months reduced the risk of death in children by 99%, reduced

the risk of death or invasive breathing assistance by 92%, and reduced the risk of death or any type of ventilation by 88%, compared to past patients without this treatment.

“This form of enzyme replacement therapy markedly extended survival and improved respiratory performance in these children, with a majority of them showing normal growth and substantial gains in motor development,” said Kishnani. “rhGAA is safe and the only effective treatment for Pompe disease; it is life saving.”

Kishnani said the young age at which the children began treatment may have contributed to their improved response compared to previous trials with rhGAA, where patients were older.

“This study demonstrates that starting enzyme replacement therapy early, which could be facilitated by newborn screening, shows great promise to reduce the mortality and disability of babies with this devastating disorder,” said Kishnani.

The most common side effects of the rhGAA treatment included skin reactions such as rash and hives, fever, and changes in heart rate. The study was supported by the Genzyme Corporation, maker of rhGAA.

For information about the American Academy of Neurology: www.aan.com. For more information about Neurology, visit www.neurology.org.

Pediatric Specialists Often Far from Home

Researchers at the University of North Carolina at Chapel Hill's School of Public Health have found that taking your child to a pediatric subspecialist may mean a big-time travel commitment.

Although about half the children in the United States live within 10 miles of most pediatric specialists, almost one in three must travel 40 miles or more to receive subspecialty care from certain physicians. The lack of available subspecialists, who are trained to treat specific ailments in children, could mean some patients are not getting sufficient care, the researchers said.

"The results suggest that the supply of pediatric subspecialists is inadequate in some locales, and the number of subspecialists is not distributed equitably," said Dr. Michelle Mayer, research assistant professor in the school's department of health policy and administration. "While we don't know to what extent these distances are barriers to subspecialty care, we think they may be problematic for low-income families with limited access to transportation or work-leave benefits."

Mayer found that the distances parents must travel to receive pediatric subspecialty care for their children range from 15 miles for neonatology (infant care) to 78 miles for pediatric sports medicine.

The results of the study, which was funded by the Agency for Healthcare Research and Quality, appear in the December 2006 issue of Pediatrics.

Researchers combined data from the American Board of Pediatrics with a national ZIP code database to calculate straight-line distances between each ZIP code and the nearest board-certified subspecialist. They used those sources to estimate the percentage of hospital referral regions with providers and calculate physician-to-population ratios for each of the 16 pediatric medical subspecialties included in the analyses.

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