Continuous Electroencephalogram Monitoring in the Intensive Care Unit

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Because of recent technical advances, it is now possible to record and monitor the continuous digital electroencephalogram (EEG) of many critically ill patients simultaneously. Continuous EEG monitoring (cEEG) provides dynamic information about brain function that permits early detection of changes in neurologic status, which is especially useful when the clinical examination is limited. Nonconvulsive seizures are common in comatose critically ill patients and can have multiple negative effects on the injured brain. The majority of seizures in these patients cannot be detected without cEEG. cEEG monitoring is most commonly used to detect and guide treatment of nonconvulsive seizures, including after convulsive status epilepticus. In addition, cEEG is used to guide management of pharmacological coma for treatment of increased intracranial pressure. An emerging application for cEEG is to detect new or worsening brain ischemia in patients at high risk, especially those with subarachnoid hemorrhage. Improving quantitative EEG software is helping to make it feasible for cEEG (using full scalp coverage) to provide continuous information about changes in brain function in real time at the bedside and to alert clinicians to any acute brain event, including seizures, ischemia, increasing intracranial pressure, hemorrhage, and even systemic abnormalities affecting the brain, such as hypoxia, hypotension, acidosis, and others. Monitoring using only a few electrodes or using full scalp coverage, but without expert review of the raw EEG, must be done with extreme caution as false positives and false negatives are common. Intracranial EEG recording is being performed in a few centers to better detect seizures, ischemia, and peri-injury depolarizations, all of which may contribute to secondary injury. When cEEG is combined with individualized, physiologically driven decision making via multimodality brain monitoring, intensivists can identify when the brain is at risk for injury or when neuronal injury is already occurring and intervene before there is permanent damage. The exact role and cost-effectiveness of cEEG at the current time remains unclear, but we believe it has significant potential to improve neurologic outcomes in a variety of settings.

(Anesth Analg 2009;109:506–23)

When a comatose, critically ill patient arrives in the intensive care unit (ICU), he or she is connected to a pulse oximetry monitor, electrocardiogram monitor, respiration monitor, arterial blood pressure monitor, and, possibly, devices to monitor arterial pressure or cardiac output, all to provide physicians and nurses with real-time information about cardiopulmonary physiology. Similar monitoring for the brain, a vital organ that is obviously dysfunctional in this case, has been unavailable to the ICU staff until recently. Typically, the patient may be examined hourly for level of arousal, motor function, and presence of brainstem reflexes, which provide only a snapshot of the neurologic status in time and assess only a small subset of important brain functions. In comatose patients, there may be too few examination findings that can be reliably followed to assess worsening brain injury. The situation is often worse for patients who are sedated and possibly paralyzed. Neurologic status is often assessed once or twice daily when sedation is lightened,[1] especially in nonneuroscience ICUs (NICU). Neuroimaging provides information about structural brain injury often after it is irreversible and cannot reveal functional changes, such as seizures and level of sedation. In addition, it often requires the transport of unstable patients. As more interventions are becoming available to treat or ameliorate neurologic injury and "time is brain," there is great need for central nervous system monitoring for at-risk patients.

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Accepted for publication February 19, 2009.

Daniel Friedman was supported by the Epilepsy Foundation William Gowers Fellowship through the generous support of Abbott Laboratories.

Lawrence J. Hirsch has received research support from GlaxoSmithKline, and honoraria for speaking from GlaxoSmithKline, Pfizer, and UCB-Pharma.

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DOI: 10.1213/ane.0b013e3181a9d8b5

Table 1. Indications for Continuous Electroencephalogram (EEG) Monitoring

1. Detection of nonconvulsive seizures and characterization of spells in patients with altered mental status with:
A history of epilepsy
Fluctuating level of consciousness
Acute brain injury
Recent convulsive status epilepticus
Stereotyped activity such as paroxysmal movements, nystagmus, twitching, jerking, hippus, autonomic variability
2. Monitoring of ongoing therapy
Induced coma for elevated intracranial pressure or refractory status epilepticus
Assessing level of sedation
3. Ischemia detection
Vasospasm in subarachnoid hemorrhage
Cerebral ischemia in other patients at high risk for stroke
4. Prognosis
Following cardiac arrest
Following acute brain injury

The electroencephalogram (EEG) provides a noninvasive way to dynamically assess brain function. Recent advances in computer technology, networking, and data storage have made cEEG monitoring practical, and its use is common in many NICUs. Methods for analyzing and compressing the vast amounts of data generated by cEEG have allowed neurophysiologists to more efficiently review recordings from many patients monitored simultaneously and provide timely information for guiding treatment. There are still many hurdles in making monitoring of brain function truly real time, reliable, practical, and widely available, but the technology is progressing rapidly. In this article, we will review the current indications and potential uses for cEEG in the critically ill (summarized in Table 1). We will also review some of the technical aspects of cEEG and address future areas of research.

DETECTION OF NONCONVULSIVE SEIZURES AND STATUS EPILEPTICUS

Nonconvulsive seizures (NCSz) and nonconvulsive status epilepticus (NCSE) are increasingly recognized as common occurrences in the ICU, where 8%–48% of comatose patients may have NCSz, depending on which patients are studied[2–11] (Table 2). NCSz are electrographic seizures with little or no overt clinical manifestations, so EEG is necessary for detection (Fig. 1, Table 3). NCSE occurs when NCSz are prolonged; a common definition is continuous or near-continuous electrographic seizures of at least 30 min duration.[12–14] Although some forms of NCSz may occur in ambulatory patients, who may appear confused, we will focus on critically ill patients for whom the most common manifestation is a depressed level of consciousness.[15] Most patients with NCSz have purely electrographic seizures[2] (Fig. 2) but other subtle signs can be associated with NCSz, such as face and limb myoclonus, nystagmus, eye deviation, pupillary abnormalities (including hippus), and autonomic instability.[15–18] None of these signs are highly specific for NCSz, and they are often seen under other circumstances in the critically ill patient; thus, cEEG is usually necessary to diagnose NCSz.

The etiologies for NCSz and NCSE in ICU patients are similar to the causes of convulsive seizures in these patients. These include acute structural lesions, infections, metabolic derangements, toxins, withdrawal and epilepsy, all common diagnoses in the critically ill patient.[19] However, NCSzs are the more common ictal manifestation in ICU patients and should be considered when evaluating the cause of or contributors to altered mental status, especially in high-risk populations. Patients with NCSz are not exclusively in NICUs; studies that have included patients who are comatose in any ICU,[4] the pediatric ICU,[7] or have unexplained altered mental status anywhere in the hospital[2,5] have found rates of NCSz between 8% and 37%, suggesting that at-risk patients can be found in any critical care setting. In this section, we will review the incidence of NCSz/NCSE in the ICU patient by diagnostic and demographic category. The major studies are summarized in Table 2. It is important to note that many of the studies are retrospective and include some patients for whom there was a high suspicion for NCSz based on prior clinical seizures, rhythmic movements, or a possibly epileptogenic injury potentially contributing to the high rates of NCSz observed in some studies.

Convulsive Status Epilepticus

In many patients who present with convulsive status epilepticus (SE), electrographic seizures can persist even when convulsive activity has ceased.[20,21] In a prospective study, DeLorenzo et al.[11] found that 48% of the patients monitored with cEEG for 24 h after convulsive SE had stopped had NCSz, and 14% had NCSE. In most of these patients, coma was the only clinical manifestation. Patients with NCSE after convulsive SE had more than a twofold greater mortality compared with patients whose seizures ended when convulsive activity stopped in this study and the Veterans Affairs Cooperative Study.[21] Therefore, cEEG should be performed on any patient who does not quickly regain consciousness after a convulsive seizure to detect ongoing seizure activity. This includes patients who are sedated and/or paralyzed

Table 2. Studies Using Continuous Electroencephalogram (EEG) Monitoring in Critically Ill Patients for Detection of Nonconvulsive Seizures

Study	Study population	EEG type	Design	*N*	Percentage of patients with any seizures (%)	Percentage of seizure patients who had NCSz only (%)
Privitera et al.[5]	Patients with altered level of consciousness or suspected subclinical seizures anywhere in medical center.	37% routine EEG[a]	Prospective	198	37	100 (32% had no subtle clinical signs)
Jordan[6]	Patients admitted to neuro ICU undergoing Ceeg.	cEEG	Retrospective	124	35	74
DeLorenzo et al.[11]	All patients with prior convulsive SE and altered level of consciousness without clinical seizure activity.	cEEG	Prospective	164	48	100 (29% NCSE)
Vespa et al.[9]	All patients with moderate to severe traumatic brain injury admitted to the neuro ICU.	cEEG	Retrospective	94	22	52
Towne et al.[4]	ICU patients in coma without clinical seizure activity.	Routine EEG	Retrospective	236	8	100 NCSE
Vespa et al.[10]	Patients admitted to neuro ICU with stroke or intracerebral hemorrhage.	cEEG	Prospective	109	19	79
Claassen et al.[2]	Patients of all ages with unexplained decreased level of consciousness or suspected subclinical seizures.	cEEG	Retrospective	570	19	92
Pandian et al.[3]	Neuro ICU patients undergoing cEEG for diagnostic purposes or for titration of intravenous therapy for SE.	cEEG	Retrospective	105	68	? (27% NCSE)
Jette et al.[7]	Patients <18 yr old admitted to ICU with unexplained decreased level of consciousness or suspected subclinical seizures.	cEEG	Retrospective	117	44	75
Claassen et al.[8]	Patients with intracerebral hemorrhage with unexplained decreased level of consciousness or suspected subclinical seizures.	cEEG	Retrospective	102	31	58
Oddo et al.[68]	Medical ICU patients without known brain injury undergoing cEEG with unexplained decreased level of consciousness or suspected subclinical seizures.	cEEG	Retrospective	201	10 (additional 17% with PEDs)	67

SE = status epilepticus; ICU = intensive care unit; cEEG = continuous EEG; NCSE = nonconvulsive status epilepticus; NCSz = nonconvulsive seizure; PED = periodic epileptiform discharge.
[a] Routine EEG is 30–45 min of recording with or without video.

during the treatment of SE for whom the level of consciousness cannot be adequately assessed.

Subarachnoid Hemorrhage

Seizures have long been recognized to be sequelae of aneurysmal subarachnoid hemorrhage (SAH). Several studies report a 4%–9% convulsive seizure rate after the initial bleed,[22–25] often in the setting of a focal clot.[24–26] Several studies using cEEG suggest that this seizure rate underestimates the incidence of electrographic seizures after SAH, especially in comatose patients. In a study of 49 consecutive patients diagnosed with NCSz,[13] 10% had SAH. In the Columbia series of 570 patients who underwent cEEG for mental status change or suspicion of seizures, 19% of 108 SAH patients monitored had seizures.[2] Most of these seizures were NCSz, and 70% had NCSE. Seizures after SAH may worsen brain injury, as both convulsive and NCSzs are associated with poor outcome in these patients.[22,27]

Intracerebral Hemorrhage

Intracerebral hemorrhage (ICH) is associated with a 3%–19% rate of in-hospital convulsive seizures.[8,26,28–31] In two recent studies using cEEG, 18%–21% of patients with ICH had NCSz.[8,10] cEEG findings may also predict outcome after ICH. Vespa et al.[10] found that NCSz were associated with increased midline shift and were associated with a trend toward worse outcomes. In the study by Claassen et al.,[8] NCSz were associated with

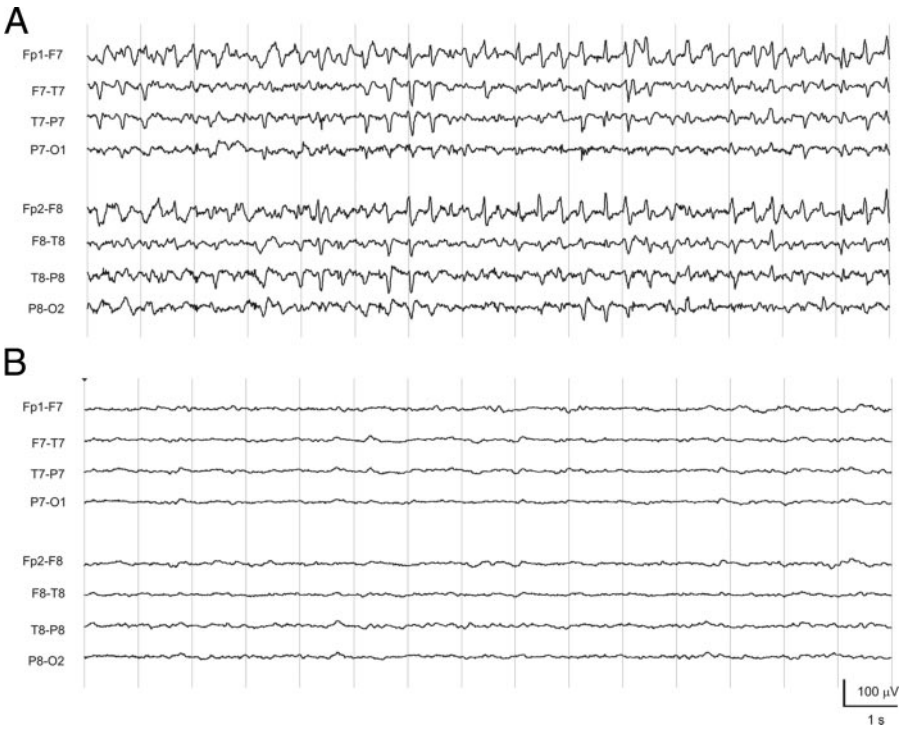

Figure 1. Continuous electroencephalogram (EEG) recording in a 70-yr-old man with recent aortic valve repair who had altered mental status in the surgical intensive care unit (ICU). A, Initial EEG reveals nonconvulsive status epilepticus with generalized epileptiform discharges at 3 Hz. B, The epileptiform discharges were abolished after the patient was given lorazepam 1 mg IV.

Table 3. Criteria for Nonconvulsive Seizure[a]

Primary criteria
Any pattern lasting at least 10 s satisfying any one of the following three primary criteria:
Repetitive generalized or focal spikes, sharp-waves, spike-and-wave complexes at ≥3/s
Repetitive generalized or focal spikes, sharp-waves, spike-and-wave or sharp-and-slow wave complexes at <3/s and the secondary criterion
Sequential rhythmic, periodic, or quasi-periodic waves at ≥1/s and unequivocal evolution in frequency (gradually increasing or decreasing by at least 1/s, e.g. 2–3/s), morphology, or location (gradual spread into or out of a region involving at least two electrodes). Evolution in amplitude alone is not sufficient. Change in sharpness without other change in morphology is not enough to satisfy evolution in morphology
Secondary criterion
Significant improvement in clinical state or appearance of previously absent normal electroencephalogram (EEG) patterns (such as posterior-dominant "alpha" rhythm) temporally coupled to acute administration of a rapidly acting antiepileptic drug. Resolution of the "epileptiform" discharges leaving diffuse slowing without clinical improvement and without appearance of previously absent normal EEG patterns would not satisfy the secondary criterion.

[a] Adapted from Chong DJ, Hirsch LJ, J Clin Neurophysiol, 2005, 22, 79–91, who modified the criteria of Young et al.[13]

expansion of hemorrhage volume and a trend toward worse outcomes as well. In addition, the authors found that periodic epileptiform discharges (PEDs) were an independent predictor of poor outcome (see Areas of Uncertainty in cEEG for NCSz section later for further discussion).

Ischemic Stroke

Estimates for the rate of acute clinical seizures after stroke range from 2% to 9% in population and hospital-based studies.[26,28,31–34] Again, several studies using cEEG have shown that this may be an underestimation of the seizure rate in this population. In the Columbia series, 11% of 56 patients with ischemic stroke undergoing cEEG had seizures; these were NCSz in all but one patient.[2] Several studies have shown that acute clinical seizures are associated with increased mortality in patients with ischemic stroke.[26,35,36] The relationship between NCSz and outcome after stroke is unknown. However, in rodent models of stroke, NCSz were associated with increased infarct volume and a tripling of mortality.[37]

Traumatic Brain Injury

Early seizures are a common occurrence after traumatic brain injury (TBI). Initial epidemiological studies suggested that the incidence of convulsive seizures within the first week after TBI is 4%–14%[38–40] and is as high as 15% in patients with severe TBI.[38,40] Because the widespread use of seizure prophylaxis after TBI, acute clinical seizures have become less common, occurring in <1% in one large study.[41] However, clinical seizures may only be part of the problem; few studies have examined the incidence of NCSz after TBI. In 96 consecutive patients with moderate or severe TBI undergoing cEEG, Vespa[42] found that 22% of patients had seizures, and half had NCSz only. In the Columbia series, 18% of the 51 patients with TBI monitored with cEEG had seizures, all of them had NCSz, and 8% had NCSE.[2] The relatively low number

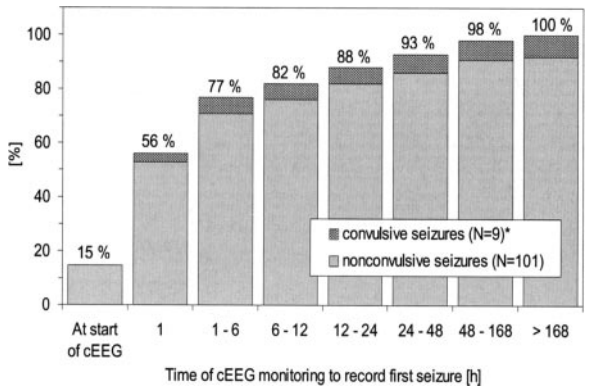

Figure 2. Summary plot of time to detect first seizure in 110 of 570 critically ill patients undergoing continuous electroencephalogram (EEG) monitoring who had convulsive or nonconvulsive seizures. Note that overwhelming majority of seizures were nonconvulsive (From Claassen et al., Neurology, 2004, 62, 1743–8, reproduced by permission).

of clinically apparent seizures in these series is possibly due to the routine use of anticonvulsant prophylaxis after TBI, but the occurrence of NCSz in these patients suggests that this prophylaxis may not be sufficient in some patients. The exact relationship between seizures and outcome is not clear, especially as early seizures are highly correlated with injury severity,[43] but some studies have shown that early posttraumatic seizures are an independent risk factor for poor outcome in adults[44] and children[45] with severe TBI. Studies have not examined whether NCSz have similar impact.

Postoperative Patients

Neurosurgical procedures, especially those involving supratentorial lesions, are associated with a 4%–17% risk of postoperative clinical seizures[46–49] depending on the indication for surgery. Patients with a presurgical history of epilepsy have a risk of postoperative seizures that has been reported to be as high as 34%.[49] Little is known about the rate of NCSz in these patients. In the Columbia cEEG series, 3 of 13 monitored postneurosurgical patients (excluding patients with SAH) had seizures, all NCSz, and 1 had NCSE.[2]

Postoperative seizures are not limited to neurosurgical procedures. They can occur in any postoperative setting, where there is a high risk of metabolic derangement, acute neurologic injury, or drug-related neurotoxicity. One particularly high-risk group is transplant patients. Seizures are common after pancreas,[50] liver,[51–54] lung,[55,56] heart,[57] kidney,[58,59] and bone marrow transplant[60,61] and often occur in the immediate postoperative period. Patients undergoing cardiac surgery are at risk for developing acute neurologic injuries, such as stroke or hypoxia[62] that may predispose them to seizures in the postoperative or perioperative period.[63] The incidence of NCSz and NCSE in these patients has not been studied. However, as in other critically ill patients with increased risk of seizures, NCSz should be considered as a cause of or contributor to unexplained mental status changes in transplant patients.

Hypoxic-Ischemic Injury

Rates of seizures have been reported to be as high as 35% after cardiac arrest.[52,64,65] In a series of comatose patients with NCSE, 42% of the patients had hypoxic/anoxic injury.[4] Twenty percent of the patients with hypoxic-ischemic injury monitored in the Columbia series had seizures, most of which were NCSz.[2] Aside from being a potential contributor to decreased mental status in these patients, the presence of seizures after cardiac arrest may have important prognostic implications,[66] as discussed later. In addition, as hypothermia after cardiac arrest for neuroprotection becomes more widely implemented, cEEG may become an important tool for identifying NCSz (especially during rewarming) and for distinguishing cooling-related shivering from seizure activity.[67]

Toxic-Metabolic Encephalopathy

Critically ill medical and surgical patients are susceptible to many toxic, electrolyte, and metabolic abnormalities that may cause both mental status changes and seizures. These include but are not limited to hyponatremia, hypo- and hyperglycemia, hypocalcemia, drug intoxication or withdrawal, uremia, hepatic failure, hypertensive encephalopathy, and sepsis.[19] In the Columbia series, 21% of patients monitored with cEEG with toxic-metabolic encephalopathy as their primary neurologic diagnosis had NCSz.[2] In other series, 5%–25% of patients with acute NCSz had metabolic derangements as the likely etiology of their seizures.[4,13] In a recent study of 201 medical ICU patients without known brain injury who underwent cEEG, 22% of patients had PEDs or seizures; sepsis and acute renal failure were significantly associated with electrographic seizures.[68]

Pediatric ICU

In the pediatric population, especially in infants, NCSz are a more common occurrence,[69] and younger age may be associated with a greater risk of NCSz.[2] Several recent retrospective studies have examined the frequency of NCSz and NCSE in critically ill children. Jette et al.[7] identified seizures in 51 of 117 (44%) pediatric patients undergoing cEEG, most of which (75%) were NCSz. The most common etiology in this study was a previous diagnosis of epilepsy. Other studies using cEEG reported NCSE in 23%–34% of patients monitored,[70,71] with prior epilepsy, hypoxic-ischemic injury, and stroke identified as the most common etiologies.[72] As in adults, seizures are an important neurologic complication of surgery as well. For instance, in a study of 183 infants undergoing surgery for congenital heart defects with cardiopulmonary bypass, 11.5% had NCSz[73] during the postoperative period.

IMPACT OF NCSZS IN THE CRITICALLY ILL

NCSzs are clearly common in the critically ill, but the evidence that they worsen outcomes and require prompt identification and treatment are mixed.[74,75] In several studies, the presence of NCSE and delay to diagnosis and treatment were each associated with significantly more frequent mortality,[9,13] although mortality in patients with NCSE may be most influenced by the underlying cause.[76] In addition, although NCSE may be associated with poor prognosis in the critically ill elderly,[77] aggressive treatment of NCSz and NCSE itself may be associated with worse outcomes in this population.[78] Because definitive proof that seizures worsen outcomes is lacking, much of the justification for identifying and treating NCSz in the critically ill comes from human and animal data demonstrating that seizures can lead to neuronal injury. There has not been a prospective controlled trial to determine whether treating NCSz or NCSE improves neurologic outcomes.

There is a large body of evidence that prolonged seizures, even if nonconvulsive, can lead to neuronal damage in several animal models. In a seminal study, Meldrum et al.[79] found that paralyzed and artificially ventilated baboons had hippocampal cell loss after treatment with a convulsant. Cell death occurred after 60 min of continuous electrographic seizures despite careful control of oxygenation, temperature, and metabolic status. Electrical and chemoconvulsant-induced SE in rodents leads to cell loss, free-radical production, inflammation, gliosis, and synaptic reorganization.[80] Pathological changes can be seen in the absence of overt convulsions and can have profound long-term effects, such as impaired performance on cognitive tasks[81] and the development of epilepsy.[82] There is also some evidence from animal models that even single or multiple brief seizures may lead to cell death and cognitive impairment.[83,84] Even in the absence of cell death, brief seizures in certain animal models can lead to alterations in gene expression,[85] impair long-term potentiation (which is related to memory),[86] and reduce the threshold for subsequent seizures.[87] SE in humans has also been associated with hippocampal cell loss in postmortem studies[88] and evidence of cell injury in hospitalized patients as demonstrated by elevated levels of serum neuron-specific enolase (NSE).[89] SE also increases the risk for developing epilepsy.[90] Although the sequelae of NCSz and NCSE are not as well understood, evidence suggests that they can lead to neuronal damage in humans. In a study of NSE levels after seizures, DeGiorgio et al.[91] showed that NSE levels were especially high after NCSz and seizures of partial onset even in absence of acute brain injury.

In addition to direct pathological effects of seizures themselves, seizure may also worsen the extent of injury from the inciting neurologic injury. Seizures can place increased metabolic, excitotoxic, and oxidative stress on at-risk brain, leading to irreversible injury. For instance, microdialysis studies in patients with TBI demonstrated increases of extracellular glutamate to excitotoxic levels after NCSz[92] as well as associated elevated lactate/pyruvate ratios and ICP.[93] Compared with patients without NCSz who had similar injuries, patients with NCSz had impaired brain metabolism and increased ICP that could be seen up to 100 h after injury.[93] As mentioned earlier, NCSz in ICH were associated with increased mass effect on serial imaging in one study[10] and expansion of hematoma size in another.[8] Seizures are also associated with increased metabolic demand, which may worsen injury to ischemic brain, particularly the penumbra. NCSz were associated with increased infarct volumes after middle cerebral artery occlusion in rats[37] and treatment resulted in reduced volumes.[94] In addition, even brief seizures can lead to hemodynamic changes, such as increased cerebral blood flow (CBF),[95] which may lead to transient and potentially injurious increase in ICP, even in the absence of tonic-clonic activity.[96,97]

DURATION OF MONITORING TO SCREEN FOR NCSZ

Several studies have addressed the duration of cEEG required to diagnose NCSz in comatose critically ill patients. In their study of NICU patients, Pandian et al.[3] found that routine EEGs (30 min) detected seizures in 11% of patients, whereas subsequent cEEG detected seizures in 28%. In 110 critically ill patients with seizures detected by cEEG, Claassen et al.[2] found that half of patients had their first seizure within the first hour of monitoring. Although 95% of noncomatose patients had their first seizure within 24 h, only 80% of comatose patients had a seizure by this time (Fig. 2). After 48 h of monitoring, 98% of noncomatose versus 87% of comatose patients had had their first seizure. In this study, both coma and the presence of PEDs (see later) predicted a delayed occurrence of the first seizure (>24 h). Therefore, monitoring for 24 h is probably sufficient to exclude NCSz in noncomatose patients without PEDs, but longer periods may be required for comatose patients.

AREAS OF UNCERTAINTY IN CEEG FOR NCSZ

The background, interictal, and ictal EEG patterns of the critically ill patient are significantly different from those encountered in ambulatory patients.[98,99] There are several periodic patterns common to critically ill patients in which the relationship to seizures is unknown.[100] Although certain periodic discharges may be more closely related to systemic metabolic abnormalities, such as triphasic waves in hepatic encephalopathy, others may reflect injured tissue at risk for seizures, such as PEDs (e.g., periodic lateralized epileptiform discharges, or PLEDs, or generalized period epileptiform discharges, or GPEDs). Furthermore, some periodic patterns may themselves be ictal. Although periodic discharges are typically felt to be interictal

Table 4. Benzodiazepine Trial for the Diagnosis of Nonconvulsive Status Epilepticus (Adapted from Jirsch J, Hirsch LJ, Clin Neurophysiol, 2007, 118, 1660–70)

Appropriate patients have rhythmic or periodic focal or generalized epileptiform discharges on electroencephalogram (EEG) with unexplained altered level of consciousness or a level of consciousness lower than expected given their level of sedation. Patients who are heavily sedated/paralyzed are not suitable as they would not be expected to demonstrate clinical improvement.
Need to monitor EEG, pulse oximetry, arterial blood pressure, electrocardiogram, respiratory rate with dedicated nurse as patients are at risk for hypotension and respiratory depression
Antiepileptic drug trial
Sequential small doses of rapidly acting short-duration benzodiazepine such as midazolam at 1 mg/dose
Between doses, repeated clinical and EEG assessment
Trial is stopped after any of the following:
1. Persistent resolution of the EEG pattern (and exam repeated)
2. Definite clinical improvement
3. Respiratory depression, hypotension, or other adverse effect
4. A maximum dose is reached (such as 0.2 mg/kg midazolam, although higher may be needed if the patient is on chronic benzodiazepines)
Test is considered positive if there is resolution of the potentially ictal EEG pattern and either an improvement in the clinical state or the appearance of previously absent normal EEG patterns (e.g., posterior dominant "alpha" rhythm). If EEG improves but patient does not, the result is equivocal.

or on an interictal-ictal continuum,[100,101] there are cases in which they are clearly ictal, such as when there is focal motor jerking with each discharge. There is some other evidence that PLEDs are occasionally ictal. Positron emission tomography in a patient with frequent PLEDs demonstrated increased regional glucose metabolism similar to that of focal seizures.[102] Single-photon emission computed tomography imaging in patients with PLEDs demonstrated increased regional cerebral perfusion that normalized when the PLEDs resolved.[103,104] In addition, frequent PLEDs in elderly patients have been associated with a confusional state that resolves spontaneously or with diazepam treatment.[105]

A common practice used to distinguish ictal from nonictal EEG patterns in the critically ill is to determine whether the periodic pattern is abolished by a trial of short-acting benzodiazepines. However, almost all periodic discharges, including the periodic triphasic waves present in metabolic encephalopathy and the discharges of Creutzfeld-Jakob disease, are attenuated by benzodiazepines.[106] Thus, unless there is clinical improvement accompanying the EEG change, the test is not helpful. Unfortunately, improvement can take substantial time even if the activity is NCSE and is aborted with benzodiazepines. However, a substantial portion of ICU patients with NCSz or NCSE improve neurologically, usually within a day of treatment. Drislane et al.[107] found that 56% of critically ill patients without anoxic injury treated for NCSzs had an improvement in mental status. Although noncomatose patients were more likely to improve (81%), 48% of comatose patients improved as well. Our protocol for attempting to prove the presence of NCSE is shown in Table 4. It is important to recognize that lack of clinical improvement does not exclude NCSE; it simply does not help determine its presence or absence.

Although there is some evidence that the presence of PEDs are an independent risk factor for worse prognosis in ICH[8] and SAH,[108] it is unclear whether these and other periodic discharges require treatment and how aggressive this treatment should be. This is currently an area of active clinical research.[42,109] In addition, laboratory studies and computer modeling are beginning to probe the network mechanisms that mediate periodic discharges in the injured brain.[110]

Another common pattern in encephalopathic ICU patients is epileptiform activity triggered by stimulation or arousals. The evoked activity may be anywhere on the interictal to ictal spectrum and we have termed it as stimulus-induced rhythmic, periodic, or ictal discharges (SIRPIDs).[111] There is usually no clinical correlate, as with most ICU seizures, but a small portion of patients will have focal motor seizures consistently elicited by alerting stimuli.[112] This is most likely a result of hyperexcitable cortex that is activated by the usual arousal pathways, which involve the upper brainstem, thalamus, and widespread thalamocortical projections. The treatment and prognostic implications of SIRPIDs are currently unknown, but the relationship between ictal discharges and arousals raises the possibility that limiting unnecessary stimulation in patients with SIRPIDs may be beneficial.

There has also been no systematic study of how drugs typically used in ICUs for sedation alter the nature and affect the interpretation of potentially ictal periodic pattern. Commonly, cEEG is performed to diagnose NCSz in patients who have unexpected depressed levels of consciousness despite not taking sedating medications. However, when cEEG is performed for differential diagnosis of abnormal rhythmic movements, especially in surgical and medical ICUs, patients are often receiving propofol, opiod receptor agonists, benzodiazepines, or dexmedetomidine, drugs which have been reported to have both pro- and antiepileptogenic effects.[113]

OTHER CHANGES IN BRAIN FUNCTION

The EEG can reveal much more about brain state aside from the presence or absence of seizures. There

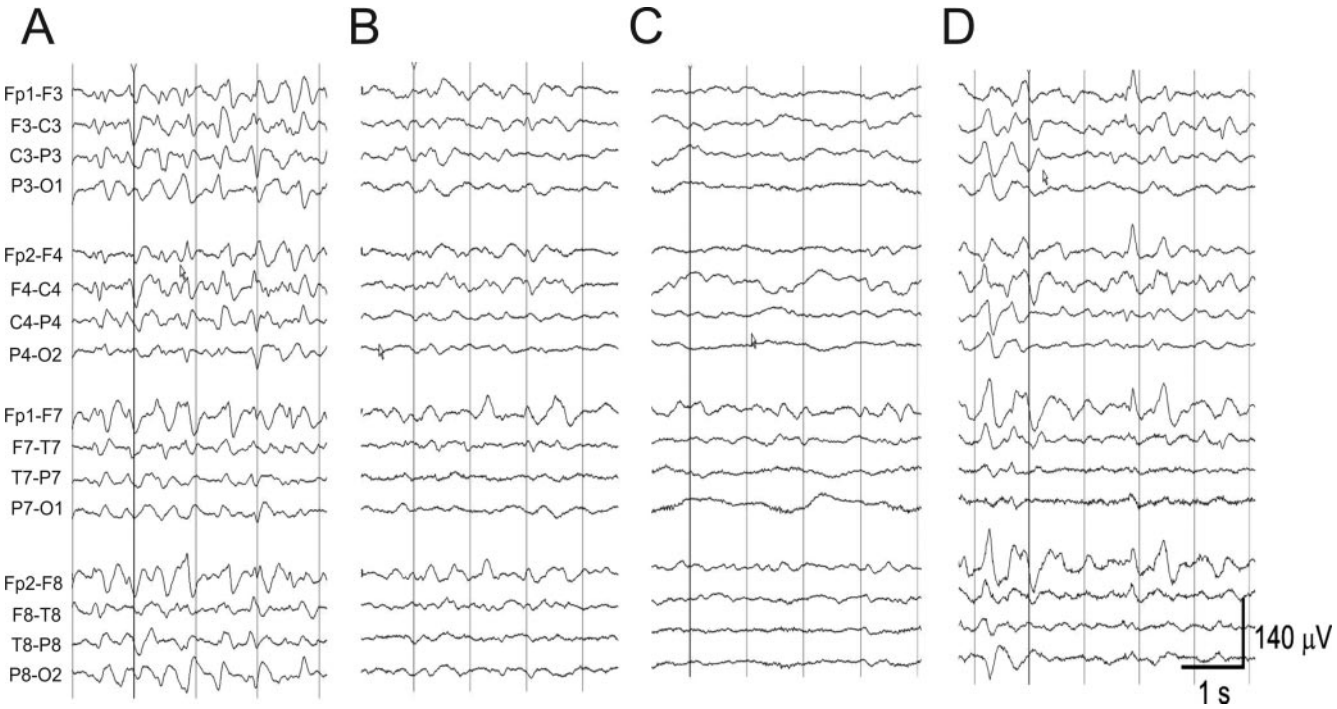

Figure 3. Detection of changes in brain physiology not due to seizures using continuous electroencephalogram (EEG) monitoring in comatose patients. This EEG tracing was recorded from a 56-yr-old woman with elevated intracranial pressure (ICP) due to cryptococcal meninigitis. A, Initial (baseline) EEG shows blunt generalized periodic discharges. A lumbar drain was placed to manage elevated ICP. B, Several hours later, there is attenuation of EEG activity. C, Ten minutes later, there is progression of EEG attenuation and the record became unreactive. The primary team was notified of the change, and it was discovered that the lumbar drain was not draining. D, After repositioning the drain, cerebrospinal fluid resumed draining, EEG reactivity returned, and the EEG gradually returned to baseline after several hours.

are distinct electrographic patterns associated with different states of arousal and with different levels of focal and global brain dysfunction and, because of the continuous nature of EEG monitoring, it is possible to assess changes on a second-by-second basis and observe trends (Fig. 3).

ISCHEMIA DETECTION

One older application of cEEG receiving renewed interest is the detection of brain ischemia due to the coupling of neuronal activity and CBF. EEG changes occur within seconds of reduction in CBF,[114,115] and this is the basis for intraoperative EEG monitoring for patients undergoing surgeries with a high risk for cerebral ischemia, such as carotid endarterectomy.[116–118] In these patients, as CBF decreases below 25–30 mL·100 g^{-1}·min^{-1} there is a progressive loss of higher frequencies and prominent slowing of background EEG activity. When CBF is below 8–10 mL·100 g^{-1}·min^{-1}, low enough to cause irreversible cell death, all EEG frequencies are suppressed.[119,120] Therefore, cEEG can detect a window in which intervention can potentially prevent permanent brain injury. This is becoming important as thrombolytics and endovascular therapies have been shown to be effective in acute stroke and vasospasm, especially when treatment is provided very early.[121,122]

Recent advances in computing have allowed for the real-time application of quantitative algorithms (qEEG) for extracting time-frequency data to measure changes in the background EEG rhythms. The ability to reduce EEG patterns usually identified by visual review to simple values allows for prolonged use of cEEG in the ICU to detect cerebral hypoperfusion, especially in comatose or sedated patients when clinical examination is limited (Fig. 4). In this section, we will review the applications of cEEG for detection of ischemic stroke and delayed cerebral ischemia (DCI) due to vasospasm after SAH. It should be noted that all of these studies examined the use of qEEG for ischemia detection in a retrospective manner and that the performance of these tools in patient management has yet to be tested rigorously; this is largely due to the lack of practical software to detect these changes in an automated fashion and the lack of true, real-time cEEG (neurotelemetry) as there is with cardiac telemetry in almost all hospitals today.

Vasospasm is common after aneurysmal SAH and causes symptomatic DCI in 36% of patients, which is associated with a 1.5 to threefold increase in mortality. Vasospasm occurs 3–14 days after the initial SAH and is diagnosed using a combination of serial clinical examinations, transcranial doppler (TCD) studies, and, possibly, less commonly used modalities, such as CO_2 reactivity and invasive tissue oxygen monitoring, all typically with angiographic confirmation as needed.[123] Once confirmed, it can be treated with a combination of hypertension-hemodilution-hypervolemia therapy,

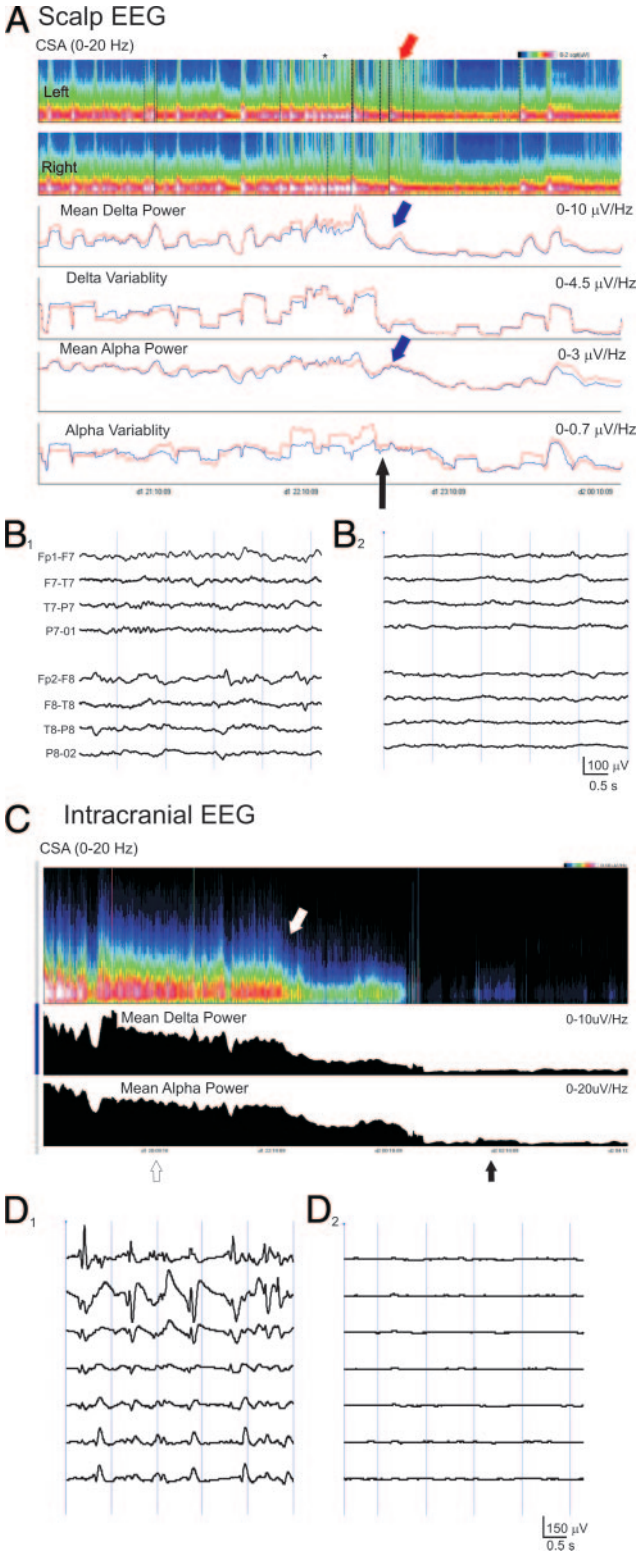

Figure 4. Use of quantitative electroencephalogram (EEG) trends to detect delayed cerebral ischemia in a comatose patient with subarachnoid hemorrhage (SAH). A, Plot of time-frequency trends over 8 h of cEEG recording includes hemispheric compressed spectral array (CSA) for frequencies between 0 and 20 Hz (top), hemispheric mean δ power (left hemisphere = blue and right hemisphere = red) and variability (middle) and hemispheric mean α power and variability (bottom). At 23:30 (black arrow), there is a persistent reduction in power in all EEG frequencies (red arrow) and a decrease in the variability of the power in the α and δ frequencies (blue arrows). The following morning, digital subtraction angiography revealed diffuse vasospasm. B, The raw EEG after 23:30 shows diffuse attenuation of electrographic activity (B_2) when compared with baseline (B_1). C, Scalp EEG recording, however, may be insensitive for detecting some of the pathological changes in brain activity. The same patient had a small intracortical multicontact depth electrode inserted in the right frontal region along with a microdialysis catheter, brain tissue oxygenation monitor, and intracranial pressure (ICP) monitor (described in Waziri et al.[169]). As in the scalp recordings, there was a diffuse attenuation of all electrical activity after 23:30. However, the reduction is much more obvious and preceded by a clear gradual trend downward for several hours in the intracranial EEG, and there is an abrupt cessation of almost all activity after 00:30. The initial gradual decrease in intracranial EEG δ power (white arrow) was seen 30 min before any changes were noticeable on scalp EEG (* in A corresponds to time of intracranial EEG changes). Subsequent imaging revealed a new area of infarction in multiple areas, including the area of the electrode. D, Baseline intracortical EEG (D_1, open arrow) reveals periodic discharges not appreciated on scalp EEG that are abolished after 23:30 (D_2, closed arrow).

intraarterial vasodilators, and balloon angioplasty. However, TCDs can detect abnormal cerebrovascular velocities at one point in time (or rarely continuously for a short period) and are often performed every 24 h. The clinical examination of a comatose patient is also limited. Therefore, cEEG-based tools are well suited to detect DCI due to vasospasm before it is apparent by current screening techniques. Several studies have demonstrated the feasibility of using qEEG for early detection of DCI. An early report using only two recording channels by Labar et al.[124] found that a reduction in total spectral power correlated with DCI and preceded clinical changes in 4 of 11 patients. In a study of 32 primarily good-grade SAH patients, Vespa et al.[125] found that a reduction in the variability of relative α frequency (6–14 Hz, expressed as a percentage of total power between 1 and 20 Hz) was 100% sensitive and 50% specific for vasospasm as detected by TCD or angiography. In majority of the patients, qEEG changes preceded the diagnosis of vasospasm by more than 2 days. In a study of 34 poor-grade SAH patients (Hunt-Hess Grades 4 and 5) monitored from postoperative day 2–14, Claassen et al.[126] found that a reduction in the poststimulation ratio of α–δ frequency power of >10% relative to baseline in six consecutive epochs of cEEG was 100% sensitive and 76% specific for DCI. A reduction of >50% in a single epoch was 89% sensitive and 84% specific. The authors examined epochs of cEEG after routine stimulation of the ICU patient by caregivers and family to minimize the variability of the EEG due to levels of sedation or sleep-wake cycles.

Patients with acute ischemic stroke can also deteriorate after their initial event due to extension of the original infarct, new infarct,[127] or reocclusion of a recanalized vessel.[128] These patients may also benefit from cEEG for ischemia detections. In a pilot study,

van Putten and Tavy[129] found that the Brain Symmetry Index (BSI), a qEEG algorithm based on the difference in the mean spectral power for 1–25 Hz between left and right hemispheres, was highly correlated with National Institute of Health Stroke Scale Scores in patients with anterior circulation infarcts. In a follow-up study, the authors also found the BSI correlated with National Institute of Health Stroke Scale changes immediately after thrombolysis.[130] Other changes in the cEEG background pattern, such as regional attenuation without δ frequency, have also been identified in patients with acute ischemic stroke[131] and may be useful for ischemia detection or prognostication.

USE OF cEEG TO MONITOR EFFICACY OF THERAPY

cEEG monitoring is especially useful in evaluating the response to interventions aimed at reducing neuronal activity to slow brain metabolism. It commonly guides the treatment of refractory SE with IV infusions of anesthetics, such as midazolam, propofol, or pentobarbital.[132] Titration of therapy to suppression of the EEG background is most effective for preventing breakthrough seizures but at the risk of hypotension.[126] cEEG may be helpful for adjusting infusion rates to maintain sufficient suppression while minimizing adverse drug effects. cEEG can also guide the withdrawal of anesthetics in these patients. Pharmacological coma has been a tool for the treatment of refractory elevated ICP in head trauma; although it can help reduce ICP,[133] it is also associated with a high risk of systemic complications, such as hypotension, renal failure, and hepatic dysfunction.[134] The use of cEEG is necessary to achieve the therapeutic goal of a suppression-burst pattern while using the lowest dose of barbiturates possible to attempt to limit adverse effects[135] (Figs. 5 and 6).

Finally, cEEG can provide information about the level of sedation in the critically ill patient, especially in the setting of neuromuscular blockade. qEEG-based tools, such as Bispectral Index,[136] patient state index,[137] and Narcotrend[138] have been in use in operating rooms and ICUs for more than a decade to monitor depth of sedation. Although these single purpose devices use proprietary algorithms, evaluation of the raw cEEG or qEEG measures can also provide information about arousal in the paralyzed patient.[139] Unlike cEEG, these devices cannot detect seizures or ischemia, and their performance has not been tested in brain-injured patients.

PROGNOSIS

cEEG monitoring can provide prognostic information after brain injury that can help clinicians and family members make treatment decisions. Prolonged monitoring can provide dynamic assessment of EEG reactivity, sleep architecture, and epileptiform discharges, which all have been found to be factors in determining prognosis for comatose patients.[140] Burst suppression patterns after hypoxic-ischemic injury are almost always associated with lack of neurologic recovery,[98] at least when therapeutic hypothermia is not used. Invariant EEG patterns that are not modulated by stimulation, such as α coma, are associated with an 88% likelihood of persistent vegetative state or death after anoxia.[141] However, this and other patterns, such as θ and α–θ coma, may be transitional; up to 20% of patients with these patterns who subsequently developed EEG reactivity recovered consciousness in one series.[142] qEEG tools, such as amplitude-integrated EEG, can also be used to predict outcome after cardiac arrest, mostly by identifying burst suppression patterns.[143] Studies have also found that convulsive and nonconvulsive SE after cardiac arrest were associated with less than a 25% chance of good neurologic outcome.[64,144] The findings of these older studies should be interpreted with caution in the era of protective hypothermia because the relationships among EEG patterns, SE, and outcome may change.[145]

EEG has also provided useful prognostic information in other clinical settings. After convulsive SE, Jaitly et al.[146] found that normalization of the EEG background was associated with an excellent outcome, whereas patterns such as burst suppression and continued electrographic seizures were associated with mortality rates of more than 50%. Many of the survivors with these patterns remained dependent. Periodic discharges also increased the risk of poor outcome, albeit to a lesser degree. In a study of 116 patients with poor-grade SAH, absence of sleep architectures and presence of PLEDs were independent risk factors for poor outcome.[108] All patients with absent EEG reactivity, generalized PEDs, bilaterally independent PLEDs, or NCSE had poor outcomes. In patients with TBI, the absence of normal sleep architecture is also a predictor of poor outcome.[147,148]

TECHNICAL ASPECTS OF CEEG MONITORING

Obtaining high-quality cEEG recordings in the ICU is a significant challenge. It is necessary to have adequate technologist coverage to connect patients and maintain those connections 24 h a day. Critically ill patients are frequently repositioned and transported to tests, which makes maintaining electrode integrity difficult. In our center, we use collodion, a durable nitrocellulose-based paste to secure disk electrodes and check the electrodes twice daily. Newer electrodes, such as subdermal wires, which may be more secure and lead to less skin breakdown, may be appropriate for comatose patients.[149,150] Concerns for image artifacts and patient safety make it necessary to remove then reapply electrodes when patients undergo brain magnetic resonance imaging, but there has been some progress in creating practical magnetic resonance imaging-compatible and computed

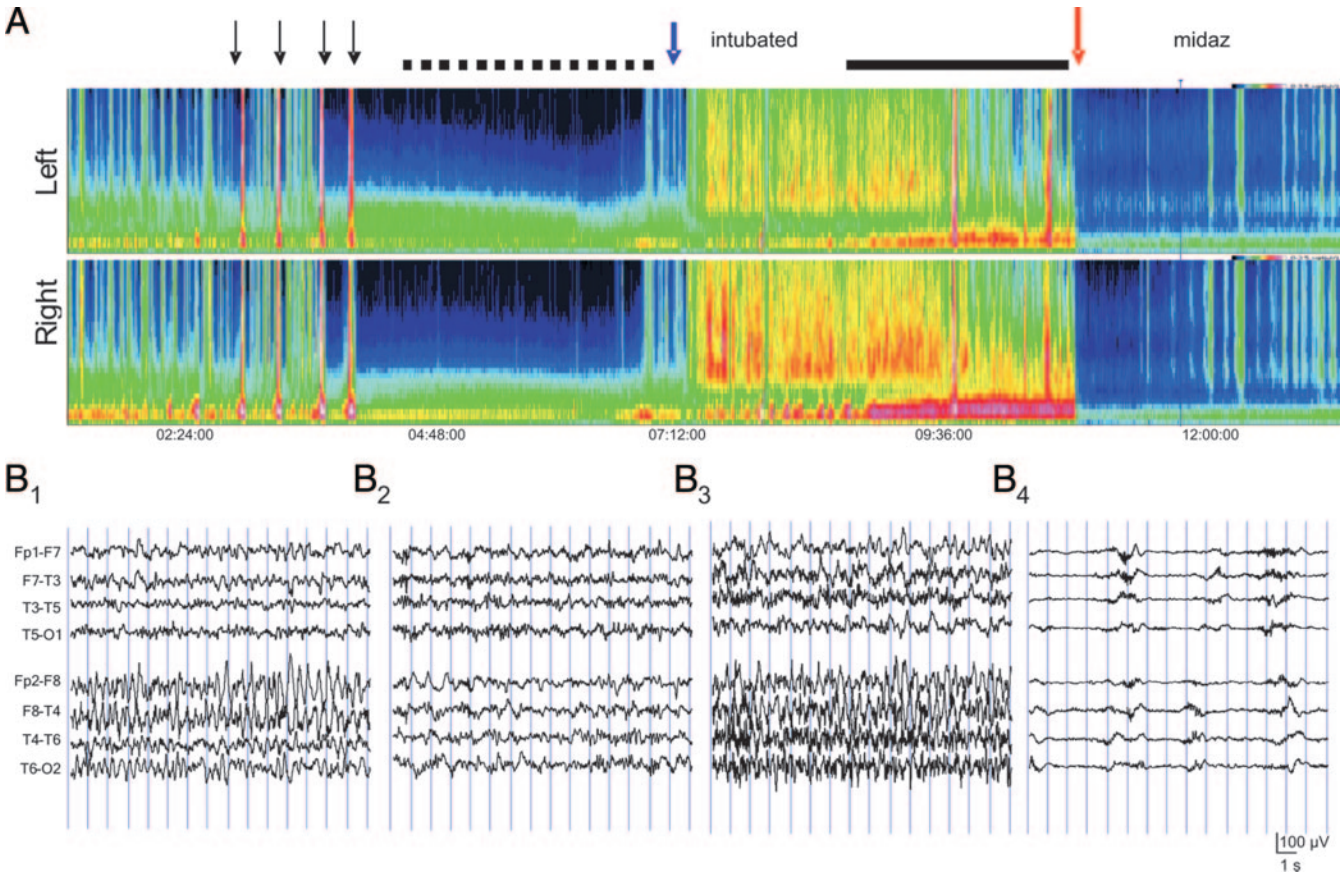

Figure 5. Quantitative electroencephalogram (EEG) tools can be used to review several hours of continuous EEG data quickly and trend pathological changes in brain function. A plot of the average hemispheric spectral power for each frequency (0–20) vs time for 12 h of recording depicts several neurologic events in a 76-yr-old patient with a small right subdural hematoma and an altered level of awareness. Transient increases of power, especially in the higher frequencies (black arrows), indicate brief right hemisphere nonconvulsive seizures (see B_1 for example raw EEG tracing). The patient was being maintained on multiple antiepileptic drugs but nonconvulsive seizures persisted. Seizures then resolved without further treatment (dotted black line and B_2). This turned out to be due to acidosis from CO_2 retention. The patient was then tracheally intubated (blue arrow), and seizures returned approximately 2 h later (just before the solid black line). Afterward, the patient progressed to nonconvulsive status epilepticus (NCSE), which appears as a prolonged period of escalating spectral power on quantitative EEG (qEEG) analysis (solid line, B_3). Finally, the patient was given an IV bolus (red arrow) and continuous infusion of midazolam, which lead to suppression of most EEG frequencies (B_4).

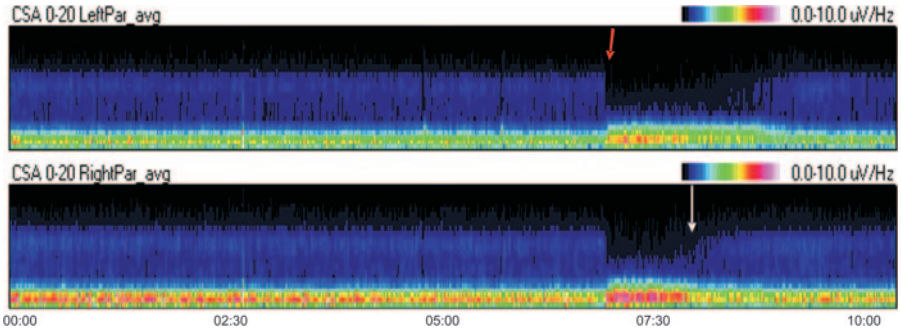

Figure 6. Plot of electroencephalogram (EEG) spectral power versus time reveals level of sedation in a patient being treated for refractory elevated intracranial pressure. At baseline, there is a mixture of θ/α (blue) and δ frequency (green on left, red on right) EEG power, with higher δ power on the right. After a bolus of IV pentobarbital (red arrow), there is an attenuation of higher frequency power (loss of blue in those frequencies) and increase in δ frequency activity (increase in red at low frequencies). As the medication wears off (white arrow), there is a gradual return of higher frequency power (return of blue) and decrease in δ power (red transitioning to green). This slow wearing off of pentobarbital effect is difficult to appreciate on raw EEG, but more obvious on long-term trend displays such as this one.

tomography-compatible electrodes.[151] These are now commercially available in the United States.

Once the patient is connected, numerous sources of artifacts make EEG interpretation difficult in the ICU environment. Some are easy to identify, such as 60 Hz (or 50 Hz in Europe) line noise from nearby electrical equipment. In some cases, it is easy to identify the source of artifact and reposition equipment to eliminate

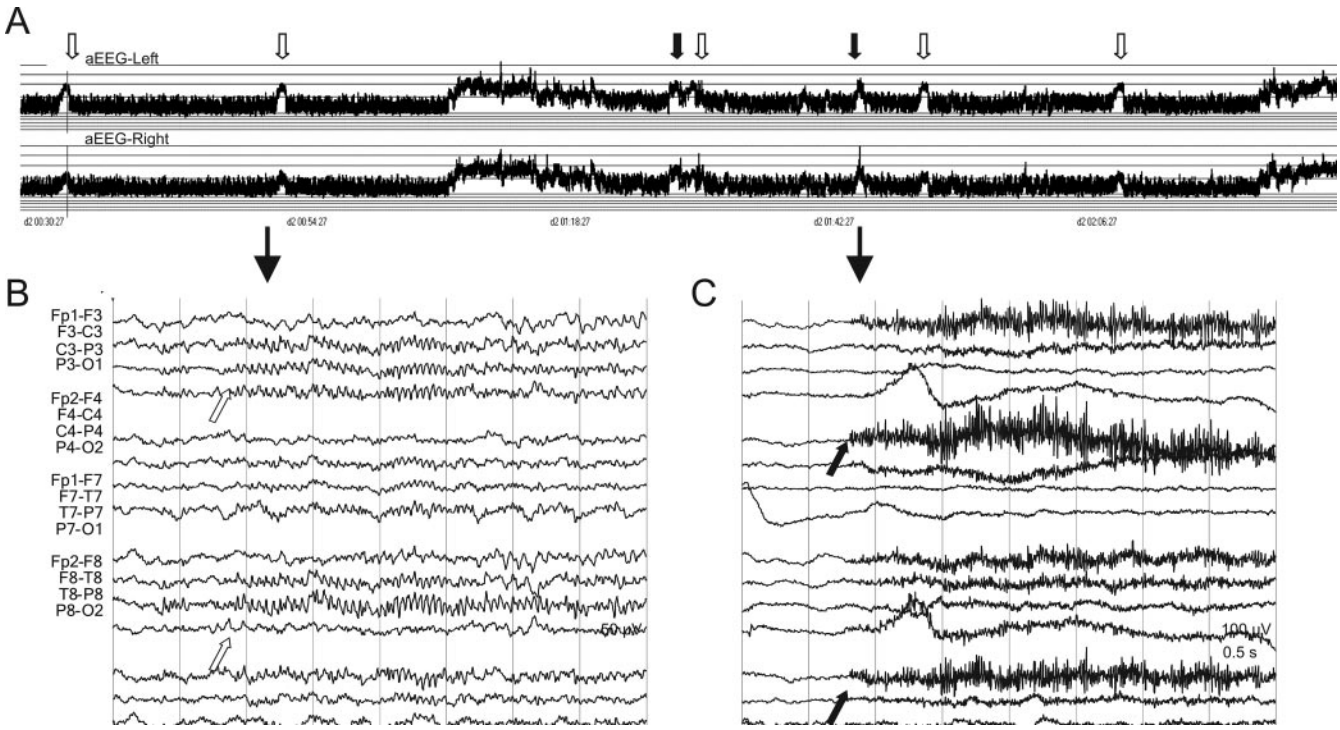

Figure 7. Limits of seizure detection using amplitude-integrated electroencephalogram (EEG). This recording was from a 64-yr-old man with central nervous system lymphoma and altered mental status. A, A plot of the average amplitude-integrated EEG (aEEG) for the left (top) and right (bottom) hemispheres demonstrates frequent transient elevations in the EEG amplitude (open arrows) that correspond to left temporal electrographic seizures. A typical seizure is shown in B, with the onset indicated by the arrows. At times, similarly shaped peaks in the aEEG trend (solid arrows) occurred that correspond to movement/muscle artifact such as that seen in C. Note that it is not possible to differentiate seizures from artifact by the aEEG tracing alone.

it. In other cases, it is impossible to remove the source of the artifact because it serves a critical function, such as dialysis machines or cooling blankets, and the reviewer can use digital filtering to minimize the artifact. The effect of filtering should be considered as it can alter the interpretation of the EEG.[150] Others artifacts, however, such as pacemakers, chest percussion, vibrating beds, and IV drips, may be difficult to avoid and sometimes mimic seizures or PEDs quite closely, causing confusion even for the most seasoned neurophysiologist.[152,153] Therefore, it is extremely helpful to record simultaneous video to help distinguish concerning brain signals from artifact, especially when reviewing cEEG remotely. The availability of simultaneous video can speed the identification of concerning patterns in patients who need immediate attention because accurate EEG interpretation can be made remotely, without having to wait for the reader to come to the bedside. In addition, video recording helps correlate EEG patterns with patient behaviors or stimulation. For instance, some significant EEG patterns in the critically ill appear after the patient is given an alerting stimulus.[111] Finally, video recording is critical to distinguish whether abnormal patient movements are due to seizures. Although clinicians at the bedside can be trained to identify EEG patterns requiring immediate intervention with the help of qEEG-based alarms (see later), confirmation by the interpreting neurophysiologist occurs after the fact and often in another part of the hospital; video recording allows the reader to place the EEG signal in the appropriate context.

The number of electrodes used in cEEG studies varies considerably. In our center, we typically perform "full electrode" recordings using 16 or more active electrodes in addition to one or two reference electrodes and cardiac leads. Other authors have used reduced electrode configurations. For instance, some studies using qEEG for ischemia detection used only eight channels.[125,129] The advantage of a reduced electrode system is that it is faster to apply and easier to maintain. It is also easier to work around other neuromonitoring devices, surgical wounds, or ventricular drains common in NICU patients. However, a full electrode configuration improves the ability to distinguish brain signals from artifact, aids in spatial localization of pathological activity, and provides redundancy, allowing continued interpretation in case one or more leads fail.[150] In addition, reduced electrode methods, especially when coupled to qEEG tools, may miss clinically significant events. For instance, Shellhaas et al.[154] found that neonatologists evaluating amplitude-integrated EEG monitoring using two electrodes for seizure detection, a technique used in purpose-built devices common in neonatal ICUs, detected only 12%–38% of seizures identified using conventional electrode arrangements. Another recent study comparing a six-electrode configuration at the hairline to a full electrode montage

found that the reduced electrode montage missed 28% of seizures and 46% of PLEDs when reviewed by experienced neurophysiologists.[155] In addition, there were false positives, perhaps more dangerous than false negatives. Reliance on qEEG tools without the ability to review the raw EEG for noncerebral signals can also lead to false-positive seizure detections (Fig. 7).

DATA ANALYSIS

Monitoring an ICU patient for several days generates gigabytes of data that, in their raw form, are nearly impossible for a neurophysiologist to review and are difficult to interpret for the nonexpert at the bedside. Computing advances have allowed qEEG tools to reduce the data and provide graphical representation of significant patterns and trends to speed review. For instance, several hours of cEEG recordings can be reduced to a single screen of time-frequency values using a compressed spectral array or density spectral array.[156] The changes in cEEG amplitude and frequency during seizures are highlighted allowing quick assessment of seizure frequency and duration (Fig. 5). Because of Internet-based networking, it is now practical to monitor dozens of patients in multiple ICUs. In addition, cEEG can be reviewed remotely from home or from a distant hospital site using virtual private networks.[150] However, in current practice, cEEG is not yet a truly real-time technology at most centers. Records are reviewed by neurophysiologists or technologists several times daily, and the presence of significant events can be communicated to the ICU team minutes to hours after they have occurred. However, the experience from two centers suggests that it is possible to train ICU nurses to accurately identify certain critical EEG patterns, such as generalized NCSE and burst suppression as well as common artifacts,[157,158] making it possible to react to these patterns early.

COST-EFFECTIVENESS OF CEEG MONITORING

cEEG monitoring can be resource intensive, especially in large medical centers, but few studies have addressed its cost-effectiveness. In a review of the early cEEG experience at University of California, Los Angeles, Vespa et al.[158] found that cEEG accounted for only 1% of the total hospital costs of 100 patients with TBI and helped guide clinical decisions in 90% of the patients. In the time period that cEEG was used, there was also a reduction in total costs and length of stay for these patients compared with historical controls, although this does not consider other simultaneous improvements in care that may have affected outcomes. In other series, cEEG was judged to make important contributions to clinical decisions in approximately half of patients.[6,159] These decisions included initiating or changing anticonvulsants in patients found to have NCSz, obtaining additional testing or adjusting mean arterial blood pressure in patients with evidence of cerebral ischemia. Although these studies suggest that cEEG often influences clinical decisions, it is yet to be proven (or even studied) that these decisions change outcomes.

FUTURE DIRECTIONS

An approachable goal is real-time application of cEEG, including using automated alarm systems at the bedside. Reducing the raw cEEG to a few displayed variables using qEEG tools will make it a practical tool that can be interpreted by nurses and intensivists. In addition, trend and critical value alarms can be used to alert the ICU staff to changes in neurologic status.[156] Computer algorithms have been successfully used to detect ongoing seizures in epilepsy monitoring unit patients.[160] Because seizure patterns in the critically ill are different from ambulatory patients, new algorithms must be designed to detect seizures in this patient population.[156] Refining techniques to help identify patterns of interest is an area of active research.[161,162] Improvement is needed because many qEEG and data reduction tools are not sufficiently specific[163] and are susceptible to contamination by artifact (Fig. 7). Although ICU staff can be easily trained to review raw cEEG traces for obvious artifacts and even pathological patterns,[157,158] a neurophysiologist must still be available to verify the interpretation. However, neurophysiologist does not need to be on site and could potentially monitor multiple ICUs in multiple hospitals simultaneously because of advances in telemedicine.

In parallel with these technical advancements, continued research is needed to confirm that real-time monitoring is a necessary goal for all applications. Although data suggest that even NCSz are injurious to brain tissue as discussed earlier, further studies need to be performed in both laboratory models and in prospective clinical trials to examine whether identifying and treating NCSz early improves outcomes. It is also necessary to determine the relationship of the different periodic and rhythmic EEG patterns in the critically ill to ongoing brain injury to identify targets for intervention.[100] Studies are also needed to determine whether using cEEG to detect ischemia improves patient outcomes and identifies the time window for intervention after a change is detected by cEEG. Such data will be necessary to justify the expense of a staff of technologists or neurophysiologists reviewing cEEG in real time much the way cardiac telemetry is performed.

cEEG monitoring is just one of the modalities available to evaluate brain physiology in the ICU. Other tools include ICP monitoring using intraventricular catheters or intraparenchymal probes, brain tissue oxygenation monitors, CBF monitoring, and brain metabolism monitoring using microdialysis probes.[164] The use of these methods in combination with cEEG may help further understanding of the complex relationships among CBF, tissue oxygenation, and neuronal activity in the injured brain. In addition, the use of

these methods together may be able to compensate for some of the shortcomings of the individual methods. For instance, microdialysis and tissue oxygenation probes sample only the area of brain into which they are inserted and can miss new injury to a remote area of the brain that may be detected by cEEG because of the wide spatial coverage. Conversely, there are situations, such as barbiturate coma, in which the relationship between EEG activity and tissue ischemia is limited and other methods may be necessary to detect new ischemic injury.[118]

Finally, further research is needed to determine whether conventional scalp EEG recording methods are sufficient for all patients. Recent studies in patients with severe TBI using subdural electrodes found episodes of cortical spreading depression, slow and prolonged peri-injury depolarizations lasting minutes, near-injured brain.[165] Similar types of cortical depolarizations have been observed in animal models of stroke, in which they are associated with infarct enlargement due to *N*-methyl-D-aspartate receptor-mediated injury.[166] Recently, these events have also been demonstrated in patients with large middle cerebral artery strokes[167] and in patients with SAH,[168] in which they have been associated with DCI. Preliminary studies at our Center[169] demonstrated that a small depth electrode inserted near-injured cortex in severely brain-injured patients was able to detect epileptiform activity and changes in background activity not readily apparent on scalp EEG. Whether targeting these events for therapy improves patient outcomes needs to be determined before more widespread application of invasive recording techniques.

CONCLUSION

In summary, cEEG is becoming an important technique for assessing neurologic status in the critically ill. Many of these patients, including those with known brain injury such as TBI, stroke, or SAH, as well as patients without structural brain injury, are at high risk for NCSz or NCSE, which can only be detected by cEEG. Therefore, cEEG should be considered not only in those with acute brain injury and impaired mental status but also in all ICU patients with unexplained alteration in consciousness, even if they do not have a history of seizures or brain injury. cEEG is also useful for titrating therapy aimed at stopping seizures or decreasing cerebral metabolism and for providing prognostic information. Finally, preliminary studies suggest that cEEG may be useful for detecting cerebral ischemia in at-risk patients. However, cEEG is an expensive and labor-intensive undertaking with risk for misinterpretation or over-interpretation and therefore inappropriate intervention. Continued education and research are needed to determine whether cEEG leads to treatment decisions that improve outcomes. Further work is also needed to reduce the cost and other resource demands of cEEG to allow widespread application. This includes software tools that can be used by the ICU staff to aid in interpretation of EEG patterns as well as hardware to allow quick and easy connection of patients to monitors.

There remain many uncertainties regarding the current implementation of cEEG monitoring in the ICU. Is imperfect EEG-based monitoring better than no monitoring at all? Although it may currently be practical to use reduced electrode systems or purpose-built devices in ICUs where technologists or neurophysiologists are not available 24 h a day, the limitations of these techniques should be well understood. There is good evidence that reduced electrode systems are not as sensitive or specific as full-lead EEG at detecting and localizing NCSz, but does the impact of missing 25% of NCSz and falsely diagnosing a small percentage with seizures outweigh early detection and treatment of the other 75% when a technologist is unavailable? More studies are needed to determine whether timely detection and treatment improves outcomes. Even if available, do all patients require full-lead EEG and neurophysiologist review? Although purpose-built devices have been shown to be effective in monitoring levels of sedation in ICU patients, they are limited to just that role. Some critically ill patients who are receiving sedation may also have brain injury or systemic conditions, such as sepsis, which put them at risk for NCSz or vulnerability to cerebral ischemia. These patients may be appropriate candidates for cEEG monitoring because of its flexibility.

Ultimately, the goal is to develop cEEG technology and our understanding of EEG patterns in the critically ill so that cEEG can be used for real-time monitoring of neurologic status. Dynamic monitoring of brain activity can help intensivists limit secondary injury in brain-injured patients and has the potential to detect neurologic injury in at-risk patients at the moment it occurs. Advances in cEEG analysis may soon make real-time bedside monitoring of brain activity possible so that neurologic status can be assessed and tracked as easily as cardiopulmonary status. The information technology infrastructure is already in place in many hospitals to make remote monitoring of cEEG possible, opening the door for true, real-time, continuous brain telemetry.

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