Neuromonitoring in the ICU

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Monitoring of patients with critical neurological illness has expanded significantly over the past several decades. Before the advent and application of technologies such as continuous electroencephalogram (cEEG), intracranial pressure (ICP) monitoring, brain tissue oxygenation, and multimodal monitoring, the care of these critically ill patients relied on frequent clinical examinations to detect subtle changes that may signal an acute neurological deterioration. This type of monitoring was limited by the availability of highly trained clinicians and nursing staff. The severity of the patient's illness can also obscure clinical changes, and then the interventions taken to treat the illness, such as induced coma for status epilepticus (SE) or intracranial hypertension, could further mask the clinical signs that would be necessary for detection of an acute change. As the field of neuromonitoring advances, there is mounting evidence to show that we can predict subtle changes that will allow for timely intervention and treatment that can prevent deterioration and secondary injury.

Continuous Video EEG Monitoring

There are numerous applications for monitoring with electroencephalography (EEG) in the neurological intensive care unit (ICU), making it a standard component of any unit. Digital recording has been in practice since the 1970s.[1] As software and networking capabilities have advanced, a standard approach to the technical considerations and staffing requirements have been described. Reliable networks, connectivity between the ICU and other locations, and EEG technologists and reviewers are all an essential part of ICU EEG monitoring.[2] The applications for EEG monitoring include: ruling out subclinical or

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INTERNATIONAL ANESTHESIOLOGY CLINICS
Volume 53, Number 1, 107–122

nonconvulsive seizures, characterizing paroxysmal clinical events, detecting cerebral ischemia, guiding medication titration, and quantifying seizure frequency in patients with SE.[3]

Seizures and Status Epilepticus (SE)

The indication for monitoring with cEEG for SE is well established. The mortality following SE has been listed to be as high as 22% at hospital discharge. In addition, the incidence of nonconvulsive status epilepticus (NCSE) after an episode of convulsive status is as high as 48%.[4–6] SE is defined as 5 or more minutes of continuous clinical and/or electrographic seizure activity, or as recurrent seizure activity without recovery in between. It is important to distinguish between convulsive SE (associated with rhythmic jerking of the extremities) and nonconvulsive SE (seizure activity on EEG without associated clinical findings).[6] This distinction is important when establishing treatment protocols, as debate still exists about how aggressively NCSE should be treated. The approach is largely guided by balancing the morbidity and mortality associated with SE and the potential for morbidity and mortality associated with aggressive treatment.[7]

The most common and well-recognized etiologies of convulsive SE are cerebrovascular disorders, brain trauma, infections, low antiepileptic drug levels in patients with epilepsy, and inflammatory processes.[8] Early treatment of convulsive status is critical in preventing a continuation of seizures and the longer it takes to provide treatment, the more refractory the seizures become.[9] Given the high frequency of NCSE following convulsive status, the use of cEEG is strongly recommended.[6]

Nonconvulsive status is seen more frequently in ICU settings as cEEG monitoring has increased. Numerous reports show that the frequency of NCSE is dependent on the etiology. The incidence of NCSE has been found to be as high as 37% in those admitted with altered mental status.[10,11] The importance of aggressive treatment of nonconvulsive seizures typically depends on the type of seizures. Animal models of absence SE would suggest that there is minimal pathologic damage from prolonged seizures.[12] There is a significant amount of evidence to suggest that severe neuronal damage from complex partial SE occurs and should therefore be treated more aggressively.[13]

The duration of cEEG monitoring for suspicion of convulsive or nonconvulsive seizures has been examined by Claasen et al[14] and shows that continuous monitoring has a sensitivity of approximately 80% after 24 hours of monitoring in comatose patients with increasing sensitivity after longer periods of monitoring. The process of seizure detection is complicated and most frequently performed by a trained neurophysiologist. A detailed review of 24 hours of continuous video EEG by direct observation has limitations. The availability of trained neurophysiologists

is limited, but is essential to accurately interpret findings and exclude artifact. An extensive review of this nature can be time consuming, with some estimates for an initial screening as high as 20 minutes, with a more detailed analysis taking much longer.[11] This type of review often cannot take place in real-time and significant delays from event to interpretation make responsive and expeditious treatment difficult.

With the advances in quantitative EEG monitoring, it becomes easier for the neurophysiologist or trained intensivist to visualize the frequency and duration of a patient's seizures. Quantitative EEG is the application of mathematical and analytical techniques to analyze EEG frequencies.[11] Once verified with the raw EEG data, these quantitative tools can be used to determine the frequency of seizures and to monitor the effects of antiepileptic medications. When ICU nursing staff is properly trained to recognize these patterns, they can be used as an alerting mechanism for the intensivist in goal-directed therapy.

Several analytic tools have become available through commercial software to allow for visualizing compressed EEG over longer periods of time. When analyzing seizures, the analysis of rhythmicity with time along the *x*-axis and frequency along the *y*-axis are useful markers. Color scales are used as a measure of rhythmicity (Figs. 1, 2, a proprietary algorithm from Persyst, Prescott, AZ). Seizure probability is derived from a seizure detection algorithm that makes a more complex integration of rhythmic patterns based on typical models on how seizures evolve. It is important to recognize that there are limitations to these computational models, especially in the ICU when rhythmic patterns can develop from ventilators, oral care, and bed percussion, and may be false positives. It is still important to have it verified by a trained neurophysiologist comparing the automated detections to the raw EEG recordings.

In cases where seizures are difficult to control, EEG becomes essential in monitoring the level of sedation and effect of medication. It is strongly recommended that the cEEG findings guide therapy in patients with refractory SE.[6] During the initial phase of treatment, the frequency of seizures is used as a marker for efficacy of first-line and second-line agents. If initial therapy has failed, the use of anesthetic agents is typically started, with medications titrated to the EEG findings. Typically, the patient is placed into a burst suppression pattern with electrographic (cEEG) control for 24 to 48 hours with intermittent withdrawal of anesthetic agents. With the use of quantitative EEG tools, monitoring the depth of burst suppression has also become easier and trained personnel can perform bedside analysis.

Prognosis and Treatment of Seizures After Cardiac Arrest

cEEG monitoring is used both to monitor for seizures and as a prognostic indicator in patients following cardiac arrest. Following

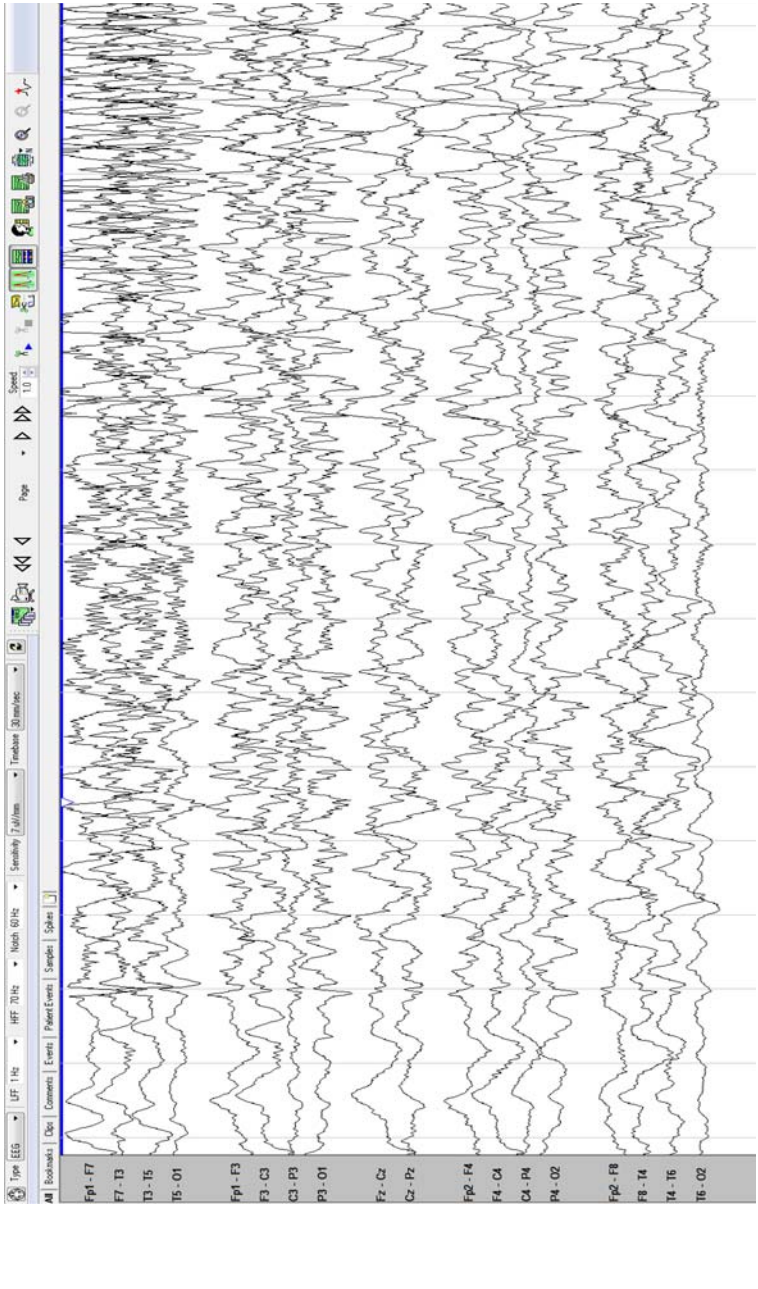

Figure 1. *Electroencephalograph (a 10-20 system with 21 electrodes) displaying in an anatomic bipolar montage, the study above shows the onset of a seizure from the left hemisphere, initially characterized by fast activity which then spreads more broadly and slows as it increases in amplitude.* full color online

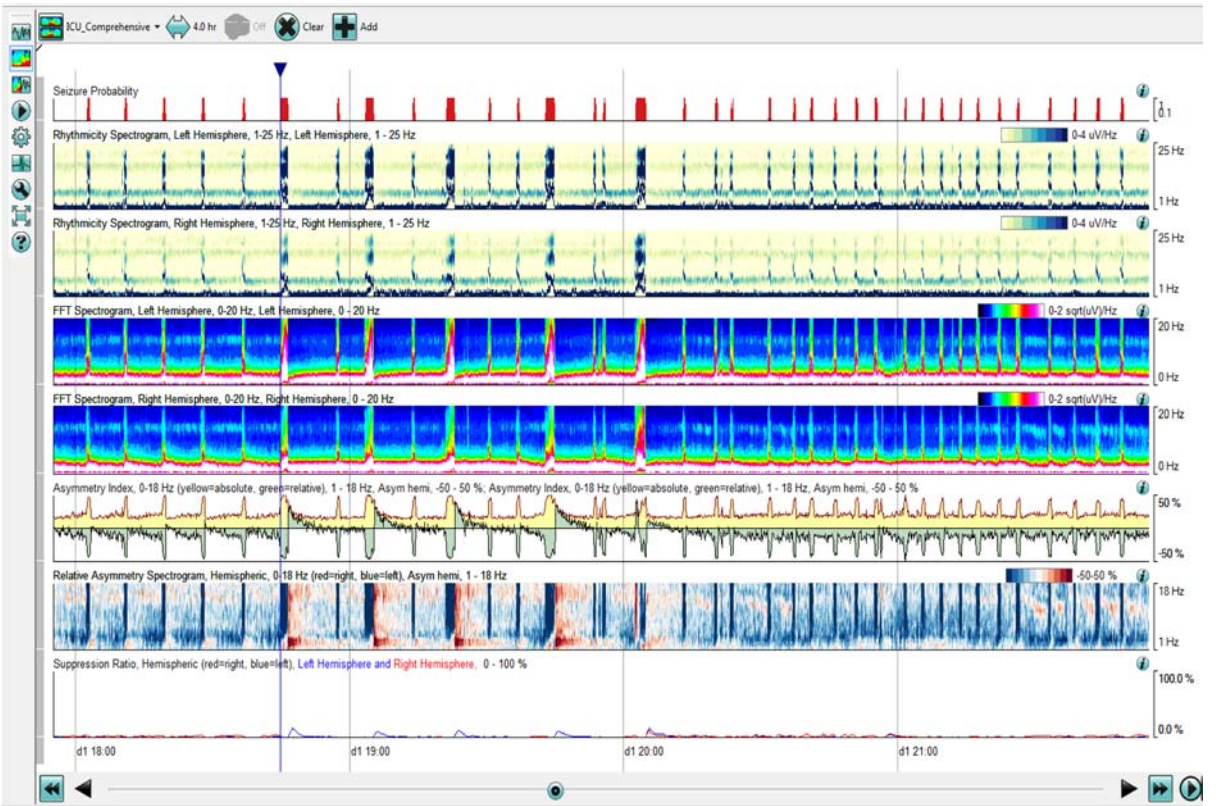

Figure 2. *Quantitative electroencephalograph of a patient in status epilepticus. There are approximately 8 to 12 electrographic seizures that occur per hour as detected through the seizure probability algorithm (Persyst, Prescott, AZ).* full color online

several landmark studies on the use of hypothermia after cardiac arrest, many institutions developed advanced protocols for treatment, which included the use of paralytics to minimize shivering.[15–17] Shivering increases the metabolic rate and can be counterproductive to hypothermia.[18] The use of paralytics to control shivering can often mask the clinical signs of seizures in this population, which is at high risk. The frequency of seizures and NCSE following cardiac arrest has been measured to be as high as 10% to 12%.[19,20] It has also been shown that SE following cardiac arrest is an independent predictor of poor outcome.[21] This finding may support the benefit of treating seizures in this population; however, no controlled trials have validated this theory.

The evidence for the use of EEG for the purpose of prognosis following cardiac arrest has unfortunately been confounded by the use of different classification systems and timing of the EEG. Initial attempts classified EEG patterns into benign, undetermined, and malignant.[22,23] The more malignant patterns of EEG are considered to be isoelectric and nonreactive, a burst suppression pattern, and a pattern of generalized periodic discharges (Figs. 3–5).

In a recent practice parameter published by the American Academy of Neurology on the use of various markers to predict outcome after cardiac arrest, meta-analysis showed that these malignant patterns were associated with a poor outcome with a false-positive rate of 3%.[24] With the advent of hypothermia, much of the prognostic value of these malignant patterns is considered controversial, and determination of whether the EEG is reactive has been thought to be of more utility. The reactivity is defined as a "clear, reproducible change in background frequency (and mostly amplitude) following auditory or noxious stimulation, regardless of the appearance of epileptiform transients (stimulus-induced rhythmic, periodic, or ictal discharges), and categorized as present or absent."[25]

Use of EEG for Detection of Ischemia and Vasospasm Monitoring

EEG has been studied as an intraoperative method to prevent neurological morbidity during carotid endarterectomy since the 1970s.[26] The utility of using EEG during carotid endarterectomy has been shown to decrease neurological morbidity and mortality (2.3% to 1.1%), as well as a reduce the frequency of carotid shunts.[27,28] EEG markers such as an increased in slow (δ) activity and decreases in amplitude can be seen as early predictors of ischemia that can then be reversed, preventing ischemic sequelae. The same concept has been transferred to the neurological ICU for monitoring vasospasm following subarachnoid hemorrhage.

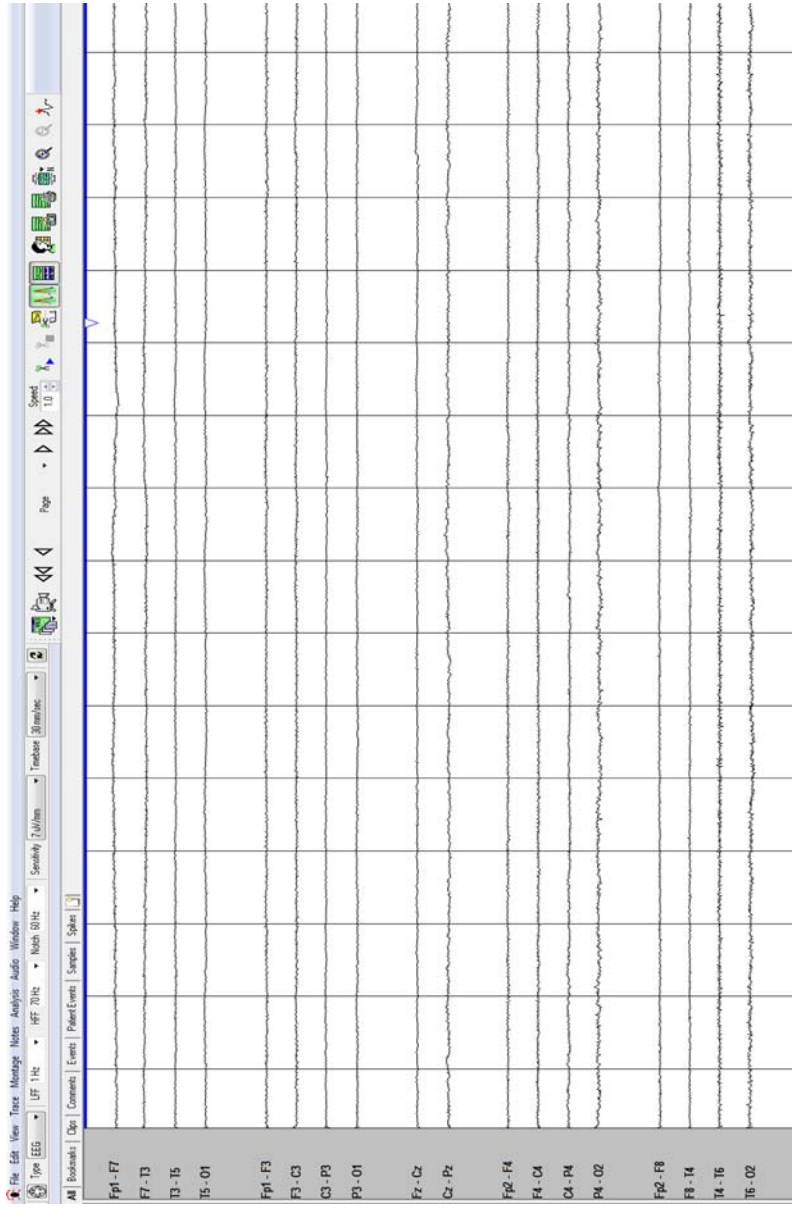

Figure 3. *An isoelectric, severely suppressed, and nonreactive electroencephalograph.* full color online

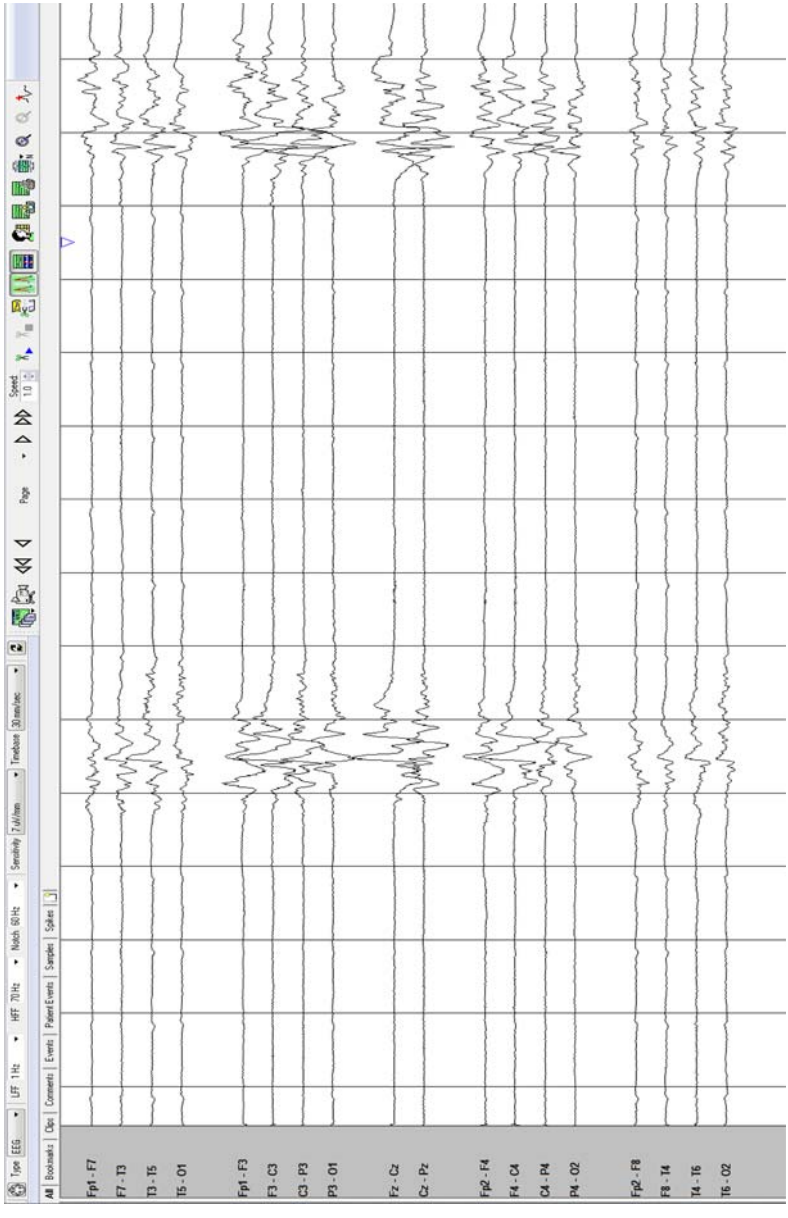

Figure 4. *A burst suppression pattern seen on electroencephalograph.* full color online

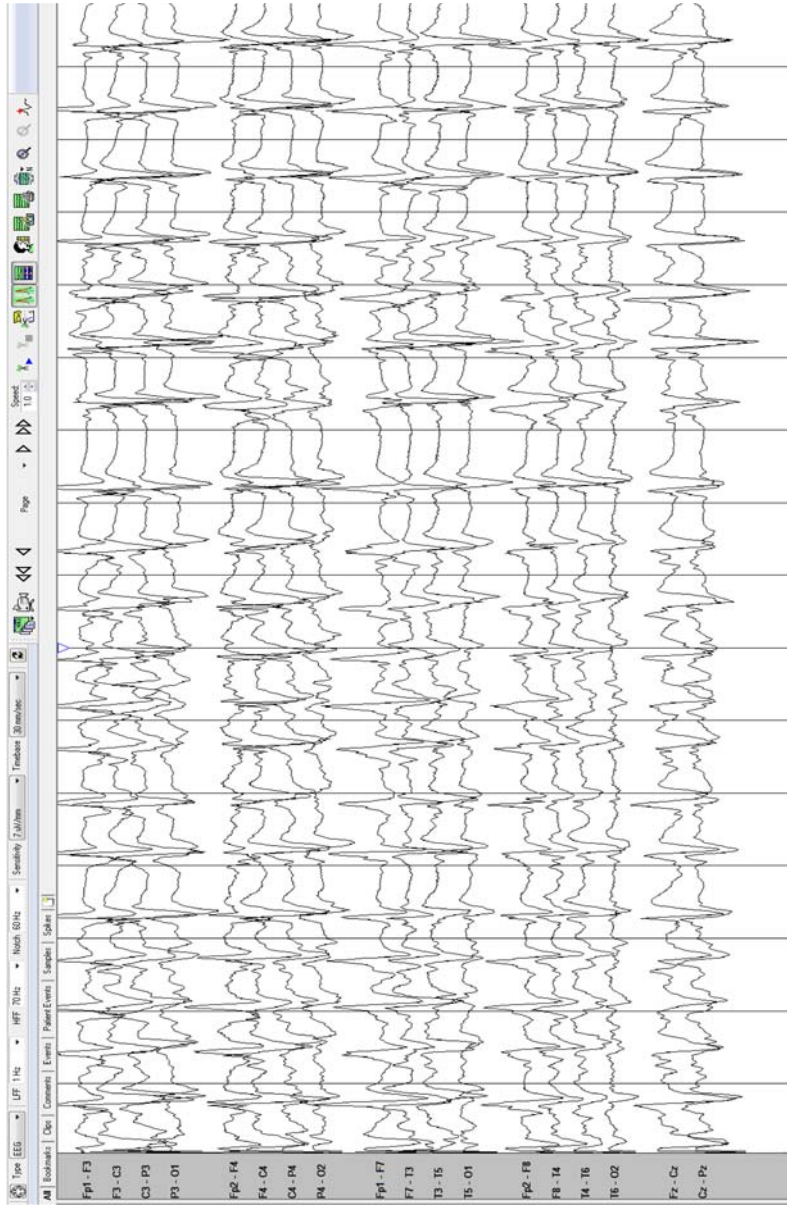

Figure 5. *Generalized periodic discharges.* full color online

Patients with aneurysmal subarachnoid hemorrhage are at risk for significant secondary injury and experience symptomatic vasospasm and delayed cerebral ischemia in 20% to 40% of cases.[29] In cases where clinical examination is limited, it can be challenging to detect a change and intervene to prevent infarction. Reductions in relative α-variability on cEEG have also been shown to be an early marker of brain dysfunction preceeding the diagnosis of angiographically documented vasospasm by a mean of 2.9 days (SD = 1.73 d).[30] Claassen and colleagues examined the most sensitive EEG predictors for vasospasm in patients with poor grade (Hunt-Hess grades 4 or 5) subarachnoid hemorrhage. The α-power/δ-power, or α/δ ratio (ADR) is a quantitative EEG measure that looks at the absolute power of a respective frequency range on the EEG. An increase in δ-frequency power becomes a sensitive indicator of the potential for cerebral ischemia[31] (Fig. 6).

■ ICP Monitoring

The basic principle of ICP is based on the Monro-Kellie doctrine that there is a fixed volume within the enclosed skull that determines the pressure. The components that make up the volume are the parenchyma (80%), the cerebrospinal fluid (CSF) (10%), and blood (10%). The individual components may change in various disease states (a hematoma, obstructive hydrocephalus), but without adequate compensation, there will be changes in ICP. One of the first and most critical considerations in monitoring ICP is recognizing what indications warrant placement of a device for this type of monitoring. Making the decision based purely on clinical grounds is typically not advised, and although the classically recognized Cushing's triad (hypertension, bradycardia, and apnea) is an indicator of intracranial hypertension, it is thought that this is likely a preterminal event.[32] An approach to deciding which disorders should be evaluated with ICP monitors is based on the conditions which typically result in ICP elevations (traumatic brain injury, aneurysmal subarachnoid hemorrhage, cerebellar strokes, encephalitis, and fulminant hepatic failure), a depressed level of consciousness, and evidence that aggressive treatment would result in an improved outcome.

Monitoring Devices

The standard ICP monitoring device is the external ventricular drainage catheter, which is connected to a pressure transducer. This is placed through a burr hole into the lateral ventricle. The device allows for both monitoring as well as drainage of CSF, which can be set at a determined level. This device has drawbacks, such as a high rate of infection (10% to 15% of patients).[33] Placement of the device is typically

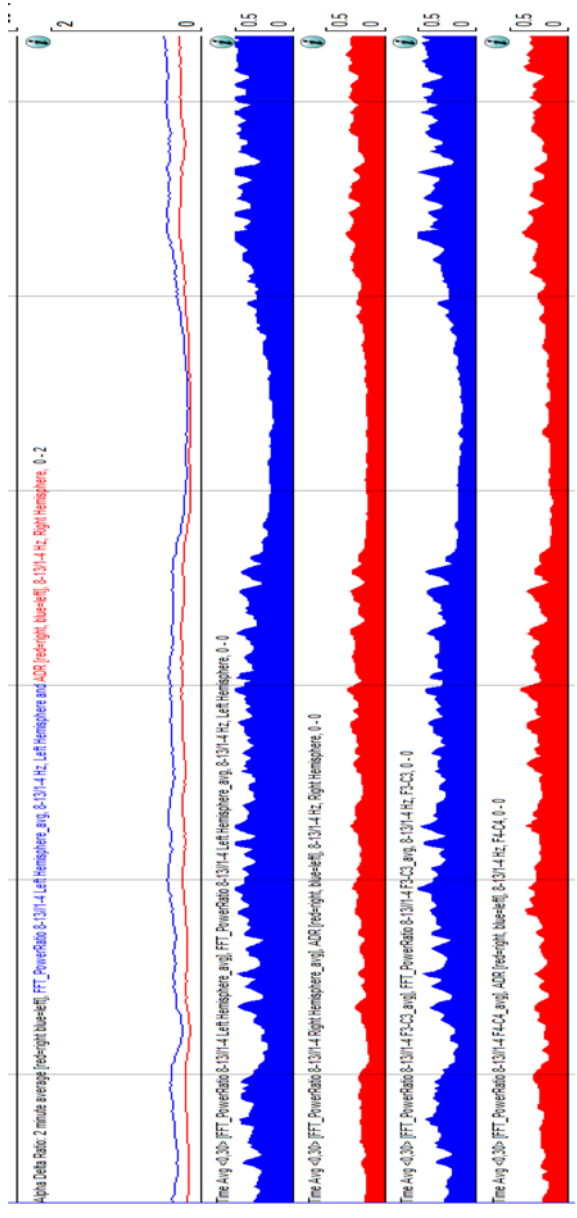

Figure 6. *The α/δ ratio difference in cerebral ischemia seen over the right hemisphere.* full color online

done by a neurosurgeon. It is placed 1 cm anterior to the coronal suture in the midpupillary line with the drain directed toward the nose 5 to 7 cm deep on the nondominant side. The transducer is then set to a stopcock placed at the level of the patient's ear.

Intraparenchymal monitors have some advantages in that they are easier to place, require minimal maintenance, and often have reliable waveforms. The drawbacks include the lack of ability to withdraw CSF and increased cost.[34]

ICP Values and Waveforms

Elevated ICP is defined as a sustained elevation of >20 mm Hg; however, there are several variables including age, body posture, and clinical conditions that can have effect on that range. Aggressive treatment is often started at 25 mm Hg.[35] During periods of ICP monitoring, there are patterns that can be seen within the waveform as trends over a longer period of time. The percussion wave is thought to originate from pulsations in the choroid plexus. The dicrotic wave is thought to be a reflection of pulsations from the major cerebral arteries followed by a tidal wave (Fig. 7). Following increases in ICP, there is an increase in the dicrotic and tidal waves beyond the percussion wave, which gives a more a rounded appearance (Fig. 8).

Plateau waves (also known as Lundberg A waves) are the result of sudden increases in ICP by 50 to 100 mm Hg that can last for up to 20 minutes. These sudden and sustained increases can often be triggered by manipulations of the patient, and often reflect a deterioration in cerebral compliance.[34] The pathophysiology behind the etiology of plateau waves is thought to be related to autoregulation in response to elevations of cerebral perfusion pressure.[36]

■ Brain Tissue Oxygenation

Brain tissue oxygen tension ($PbtO_2$) is a marker of the balance between oxygen delivery and oxygen consumption in the brain cells. Using a small electrode, the extracellular fluid is measured with normal values ranging from 25 to 35 mm Hg. Completed infarction or dead brain tissue typically has a value <5 mm Hg. It is the range between 5

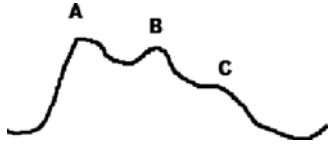

Figure 7. *A normal intracranial pressure waveform; (A)—percussion wave, (B)—dicrotic wave, (C)—tidal wave.*

Figure 8. *Elevations in intracranial pressure produce reduced compliance.*

and 25 mm Hg which is thought to reflect possible regions that are at risk. Once determining regions at risk, there is a push to apply appropriate treatments to improve outcome. In a systematic review of the use of $PbtO_2$ monitoring in traumatic brain injury, hypoxia (as defined as <10 mm Hg) was associated with worse clinical outcomes and showed that the use of the devices was safe.[37] In studies of subarachnoid patients who had frequent decreases in the partial pressure of oxygen, their outcomes were worse.[38] Because of these findings, there is a recommendation from the Brain Trauma Foundation that $PbtO_2$ is monitored, and that appropriate treatment strategies be instituted if the oxygen tension levels fall to <15 mm Hg.[39]

■ Cerebral Microdialysis

The placement of a miniature microdialysis catheter in the brain parenchyma can offer additional insight into the microenvironment and cellular metabolism. The commercial assays that are available include glucose, lactate, pyruvate, glycerol, and glutamate; however, multiple other substrates can be examined. Analysis is typically done in the parenchymal region that is considered to be at risk. Much of the literature to this point has been focused on looking at patients with subarachnoid hemorrhage and traumatic brain injury. Typical patterns which are consistent with ischemia would be diminished glucose and an increase in the lactate:pyruvate ratio.[40,41]

■ Multimodal Monitoring

Combining the methods discussed above could have potential to reveal even more clinical information about the brain-injured patient and is being used to attempt to detect subtle changes that may occur before injury. This information may prove to have significant treatment implications. An example would be in the detection of patterns on cEEG monitoring which may or may not be electrographic seizures. With changes in oxygen tension and elevations in the lactate:pyruvate ratio, what may have been considered as poorly defined EEG patterns with undetermined clinical significance could now correlate with evidence of tissue at risk.[42] Another clear example would be a pattern consistent with ischemia in a patient with subarachnoid hemorrhage. cEEG would show a decrease in the ADR, whereas brain tissue oxygenation would go

down and the lactate:pyruvate ratio would increase.[43] Some centers are now using a combination of transcranial Doppler and cerebral perfusion pressure to extrapolate individualized cerebral autoregulation. These data could potentially help find individualized therapeutic targets for arterial blood pressure in the brain-injured patient.[44] The large amount of data generated from this multimodal monitoring may reveal patterns consistent with tissue at risk that were previously undetected, and may result in bedside alerts that allow for more timely intervention.

■ Conclusions

The detection of clinical changes in the patient in the neurological ICU has evolved over the past few decades to the point where we can now detect acute processes and potentially intervene before further deterioration. There is still a significant institutional difference in how monitoring applications can be used in the neurological ICU. The use of cEEG for SE is considered the standard of care, whereas more experimental techniques such as vasospasm monitoring with cEEG and cerebral microdialysis are still considered experimental but may provide further insight into tissue at risk for further injury in the future. Development of specialized neurological ICUs has propelled the field of neuromonitoring, which will likely continue to grow over the next few decades.

The NIH grant K08 NS078048 is awarded to Dr Khalid A.Hanafy.
The authors have no conflicts of interest to disclose.

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