

Multimodality monitoring and telemonitoring in neurocritical care: from microdialysis to robotic telepresence

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Purpose of review

This review will highlight the state-of-the-art in brain monitoring in neurointensive care and define methods of integrating this technology into patient care using telemedicine methods.

Recent findings

Several new methods of brain monitoring have been established over the last several years including continuous EEG monitoring, brain tissue oxygenation, jugular venous oxygenation, and cerebral microdialysis. Observational research using these monitors has documented that the brain metabolism, blood flow and function are dynamic after a primary insult. The dynamic nature of the brain can predispose the brain to secondary insults that can occur in the setting of intensive care. Several variables of brain metabolism and function can be monitored and directly impact treatment decisions as well as provide diagnostic and prognostic information. General treatment guidelines for brain injury and brain hemorrhage were developed, in part, prior to implementation of use of these monitors, and there is a trend away from adoption of a one-size-fits-all approach and a trend towards monitor-guided therapy. Dealing with the data provided by multimodality monitoring can be overwhelming. Efficient use of such information requires methods to integrate diverse sets of information, and methods to access the online monitoring information remotely and at any time, day or night. Such remote access integration methods will be reviewed.

Summary

Multimodality and telemedicine techniques have advanced the state of knowledge about brain function in critically ill patients, and are presently being implemented to direct therapy. Increasing complexity of care will become commonplace, but will be facilitated by computer-enhanced tools that permit the intensivist to integrate this information into an improved treatment regimen.

Keywords

brain monitoring, multimodality monitoring, neurointensive care, telemedicine methods

Abbreviation

cEEG continuous electroencephalography

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Introduction

Neurocritical care for central nervous system injury from trauma, stroke, or brain hemorrhage requires specific and timely diagnosis, monitoring, and treatment based upon specific information gathered from the brain. Early after injury the brain experiences increased vulnerability to secondary insults. These insults can take the form of cytotoxic brain edema, repeat ischemia, fever-related injury and seizures, just to name the most common ones. Secondary insults are frequently silent and are expressed only once the problem becomes critical. The timely diagnosis of these secondary insults is important to overall survival of the brain. Multimodality monitoring refers to the tracking of several parameters of brain physiology and function that can be affected by direct medical or surgical intervention. These parameters include brain electrical activity (continuous electroencephalography – cEEG), brain oxygenation (jugular venous and brain tissue oxygen partial pressure – PbrO₂), neurochemistry (cerebral microdialysis), intracranial pressure, and cerebral blood flow monitoring (transcranial Doppler ultrasound). Monitoring of the brain requires the sometimes conflicting requirements of being sensitive yet specific, regional yet global, and immediately accessible yet remotely available. In the past 18 months, several publications have called our attention to this emerging field and provide guidance in the application of these important new tools to critical ill neurologic patients.

Intensive care unit continuous electroencephalography

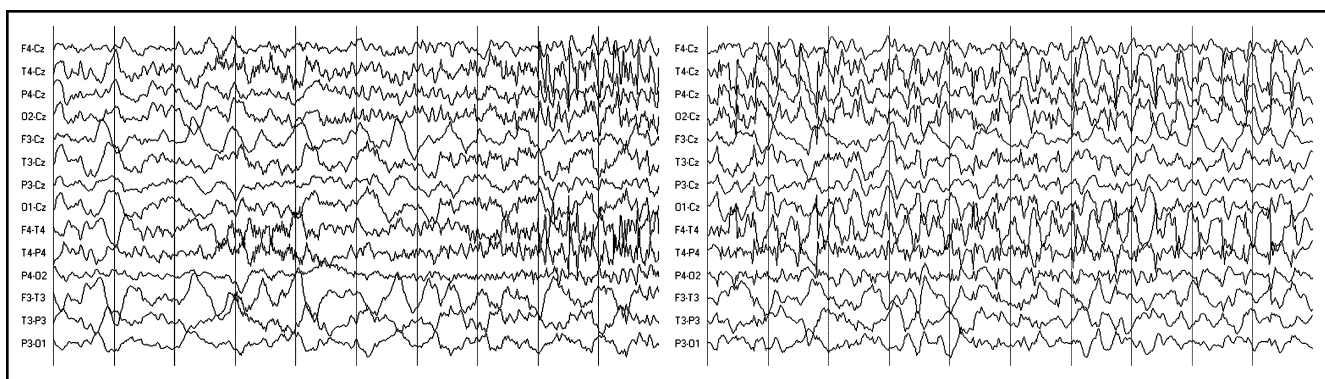
Over the past 5 years, it has become increasingly apparent that seizure activity commonly occurs in critically neurologic patients. Vespa *et al.* [1] initially demonstrated that over 20% of patients with traumatic brain injury demonstrated seizures while in the ICU, half of which were non-convulsive seizures that were detected only by the use of continuous EEG (cEEG) (Fig. 1). These seizures can be regional in the area of the primary insult, such as adjacent to a temporal lobe contusion, or can be more widespread

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Figure 1. Segment of an electrographic seizure obtained during continuous EEG monitoring

The seizure begins in the right temporal lobe, indicated F4-T4, and spreads over time to involve the entire right cerebral cortex. Each box indicates 10 seconds of EEG.

and involve the entire brain. Posttraumatic seizures were related to the severity of injury, tended to occur within the first few days after injury (despite prophylactic anticonvulsants), and were associated with increased mortality if they could not be controlled. Operational parameters for optimal brain cEEG have been established, but some variability still exists [2]. In a similar study, Vespa *et al.* [3] demonstrated that over 26% of patients with nontraumatic intracerebral hemorrhage demonstrated seizures on cEEG, and that these seizures were independently associated with progressive brain edema and midline shift. Thus, the seizures may be eliciting progressive secondary injury and promoting clinical deterioration. Figure 1 demonstrates an electrographic seizure taken from cEEG. Laboratory studies [4] as well as clinical data [5] now confirm that posttraumatic seizures are not benign and may lead to additional neurologic injury and cell death, especially in vulnerable regions of the brain such as the hippocampus. Identification of seizures and early treatment may preclude such secondary deterioration. In a similar report from another major neurocritical care center, Claassen [6] used similar cEEG methods, and detected an 18% incidence rate of seizures in a mixed population of intracerebral hemorrhage, subarachnoid hemorrhage and ischemic stroke. The seizure rate in brain hemorrhage patients was higher than that in ischemic stroke [3], which may be due to the toxicity of intraparenchymal blood and pro-epileptic effects of iron deposition in the brain. Pandian *et al.* [7] reported that combined video-EEG monitoring was useful in detecting seizures in the ICU in patients whose presenting problem was status or encephalopathy related to seizures. A similar incidence (18%) of electrographic, nonconvulsive seizures was found in this group. The addition of video information about clinical behavior confirms the previous findings that many seizures can be subclinical and therefore not detectable by clinical manifestations alone. Thus, seizures occur after primary brain injury, appear to be related to progressive

neurologic damage, and can be easily detected by available cEEG methods.

The hurdles to performing cEEG include: (a) available expertise in reading EEG, (b) automated seizure detection, and (c) remote access to EEG for real-time reporting. Several new digital EEG instruments are currently available that provide for remote access as well as automated seizure detection. This approach has been useful in our hands, and we have launched an Internet-available remote expert review system that permits remote access and assessment of the EEG. This telemedicine approach has resulted in decreased interval between event detection and intervention. Paging-enabled systems can alert the expert to assess the EEG and provide real-time assessment of recent electrographic events. Direct physician feedback to nurses or other physician-colleagues in the form of confirmation of seizure detection and record review, as well as the ability to teleconference, increases accuracy of seizure detection. In addition, the telemedicine approach creates the potential for expanding the limited list of experts to centers that presently lack the necessary in-house expertise.

Cerebral oxygenation

Preserving cerebral oxygenation in the setting of brain injury, edema and potentially secondary injury is of paramount importance in the critically ill brain. Several lines of evidence from clinical brain injury research suggest that ischemia occurs frequently in traumatic brain injury. The initial 12 hours after injury appear to be most critical, and brain oxygenation monitoring studies have demonstrated a 30% incidence of brain ischemia in the brain injury population over this time frame. Moreover, autopsy series have demonstrated that necrotic cellular changes are frequent in fatal TBI and these changes are thought to be due to ischemia, rather than other mechanisms of cell death. Recent PET studies done in TBI patients, both early and late after the injury,

demonstrate that brain ischemia can occur, especially with provocative maneuvers such as hyperventilation. Diringer *et al.* [8] performed PET studies at a mean of 12 hours post injury and demonstrated areas of potential ischemia. Similarly, Coles *et al.* [9^{*}] used ¹⁵O₂ PET studies in TBI patients and found that at baseline PaCO₂ of 30–34 mm Hg, the mean ischemic brain volume was 67 ml. This volume of ischemic brain tissue increases with provocative hyperventilation and potentially can lead to permanent tissue injury. Excessive hyperventilation can promote brain ischemia and increase the volume of tissue that is in the ischemic range. Thus, the injured brain is at high risk of ischemia, and monitoring the brain during intensive care unit treatment adjustments, such as modifying the mechanical ventilator, requires an assessment of brain oxygenation. Until recently, cerebral perfusion pressure (CPP) has been used to estimate the degree of cerebral blood flow and to avoid ischemia. However, several studies have questioned the validity of CPP [3,5,10]. Most recently, perfusion computerized tomographic imaging, performed early after brain injury, has demonstrated that the expected relationships between CPP and cerebral blood flow do not hold, with some patients having ischemic range cerebral blood flow despite CPP > 70 mm Hg [10^{*}], and that the degree of pressure autoregulation is impaired and cannot be predicted based upon baseline values of cerebral blood flow or CPP. Thus, direct monitoring of tissue oxygenation and oxygen utilization appears to be better than monitoring CPP alone to determine the adequacy of cerebral oxygenation.

There are presently two clinically available modes of brain oxygenation monitoring: jugular venous saturation (SjO₂) monitoring (a global method) and brain tissue oxygen (PbrO₂) pressure monitoring (a regional method). SjO₂ monitoring has been well established to have prognostic significance and clinical utility in detecting ischemic as well as excessively hyperemic states of cerebral blood flow and oxygen supply. Indeed, hyperemia has been reported to be the most common disturbance of cerebral blood flow as associated with alteration of brain metabolism [11], in which cerebral blood flow is increased disproportionately to the need for oxygen utilization. Oxidative metabolism (CMRO₂) is uniformly reduced after brain injury, and the extent of reduction in CMRO₂ is a significant prognostic indicator. Hyperemia is thought to occur because of impaired cerebral autoregulation and has been associated with poor outcome, especially in pediatric brain injury populations [12^{*}]. The ability to monitor cerebral blood flow in real time, and to adjust blood pressure and ventilation parameters to avoid either extreme of hyperemia or brain ischemia has become a powerful tool in the treatment of global brain edema resulting from brain injury.

In contrast to global cerebral oxygenation monitoring, PbrO₂ monitoring provides regional assessment of oxygen-

ation, in the format of a brain sensor that resembles an intracranial pressure monitor. The PbrO₂ value is thought to represent the partial pressure of oxygen in the brain, and is considered a marker of the balance between oxygen supply and utilization. The PbrO₂ is not a measure of oxidative metabolism per se, but in general can reflect changes in oxygen utilization as a function of the oxygen supply. In the last year, several interesting papers on PbrO₂ have been published and have resulted in several new concepts.

1. PbrO₂ can decrease even in the setting of adequate cerebral perfusion pressure. Menzel *et al.* [13] noted concurrent transient drops in PbrO₂ when CPP decreases below 70 mm Hg. Since it is generally agreed that PbrO₂ reflects that balance of supply and demand of oxygen in the brain, these data suggest that a CPP below 70 mm Hg results in a critical limitation of oxygen supply compared with ongoing demand. In similar studies of combined PbrO₂ and CPP monitoring, a lower CPP threshold of > 60 mm Hg was found to be the critical threshold. Indeed, studies of the variable effects of different vasopressors on the effect of brain oxygenation are now being undertaken [14].
2. Decreases in PbrO₂ are not benign and have been closely associated with independent neurochemistry markers of brain ischemia. Recently Robertson *et al.* [15^{*}] have documented that reductions in PbrO₂ below 10 mm Hg, the critical threshold of brain oxygenation, result in increased glutamate levels and reduced glucose levels in the brain. Thus, a decrease in PbrO₂ indicates critical ischemia to the brain.
3. A critical PbrO₂ threshold of 10 mm Hg has been validated in studies of prognosis after brain injury and in physiologic studies.
4. PbrO₂ increases with supplemental oxygen, and in turn, this increase in PbrO₂ is associated with improvement in brain metabolism. Niklas *et al.* [16] demonstrated that hyperbaric oxygen results in increased PbrO₂, and clinical studies by Tolia *et al.* [17^{*}] have demonstrated that increased inspired oxygen results in PbrO₂ and improvement in brain microdialysis markers of metabolism. This finding suggests that the brain may not have adequate oxygen delivery despite normal arterial oxygen content. Thus, an increase in arterial oxygenation results in not only increased local PbrO₂ but also an improvement in indirect markers of oxidative metabolism. This concept is quite controversial since direct measures of oxidative metabolism in humans have not yet been done. In fact, monitoring PbrO₂ during prone positioning or other maneuvers to increase arterial oxygenation provides direct guidance to treatment endpoints in patients with hypoxemia resulting from acute lung injury [18^{*}]. Nonetheless, it appears that the PbrO₂ monitor is a potentially important monitor for the treatment of patients with brain injury and subarachnoid hemorrhage [19,20^{*},21,22].

Brain microdialysis

Coupled with monitoring of brain oxygen has been the burgeoning clinical field of monitoring brain neurochemistry using cerebral microdialysis. Cerebral microdialysis permits the sampling of metabolites and aminoacid neurotransmitters from the extracellular space and has been validated in experimental studies to reflect changes in brain metabolism. Cerebral microdialysis is currently being used as a clinical monitor, after several seminal studies [23,24] demonstrated persistent metabolic changes occurring after brain injury. Cerebral microdialysis is often used, in conjunction with PbrO_2 , to determine if brain ischemia or other alterations in metabolism exist. In the past year several findings have begun to crystallize data pointing to the importance of this monitor:

1. Extracellular glucose is reduced after traumatic brain injury and may be related to poor outcome [25*]. These reductions may be due to ischemia, or to increased utilization of glucose. However, the pathophysiology of these changes is not completely understood, and the available evidence does not clearly indicate ischemia as a cause.
2. The lactate/pyruvate ratio is a good discriminator of altered brain metabolism or ischemia, and can be used in the setting of subarachnoid hemorrhage to diagnose and track cerebral vasospasm [26,27*,28,29,30*], with increases in the lactate/pyruvate ratio or the lactate/glucose ratio being sensitive and specific indicators of brain ischemia associated with vasospasm. Precise thresholds for diagnosing pathology using these parameters have not been agreed, and some groups

have used relative percent changes as the indicator for ischemia, whereas others have used absolute thresholds. Validation of such specific thresholds is yet to be done, but is needed to make best use of this technology in the future.

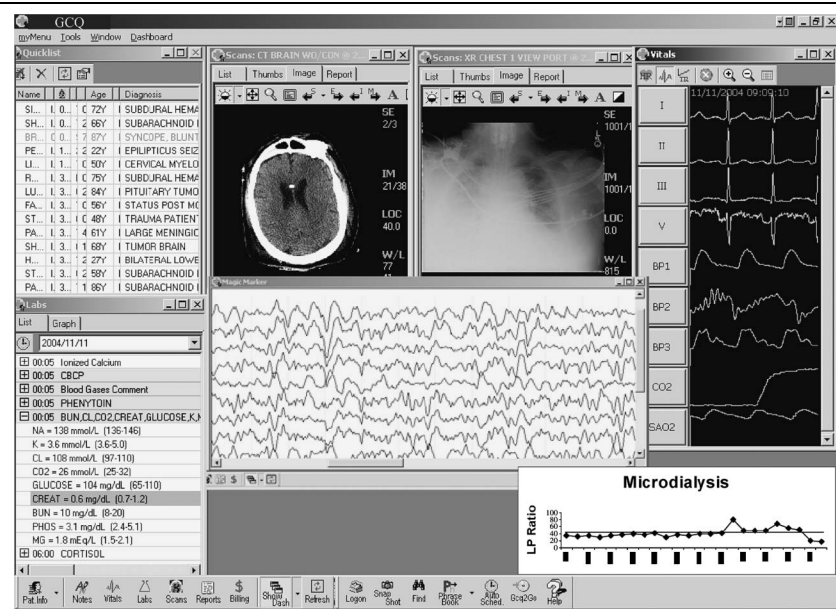
3. Results from cerebral microdialysis vary depending on the tissue in which it is performed. Pericontusional tissue appears to have different levels of metabolites compared with normal appearing brain tissue [5,30,31*]. Thus, selection of the site in which monitoring is to be performed, as well as the specific methodology of microdialysis, such as the perfusion and sampling rates, are critical factors that must be considered to perform this technique with validity. An excellent review by Hillered outlines these and other current concepts in cerebral microdialysis [32].

Telemedicine

Incorporating these new technologies into a useable system that is both accessible at the bedside and available remotely is a significant challenge. In our center at UCLA, we have approached this challenge with the use of several integrated systems. The first is an Internet web-portal for remote access to online vital signs including imaging and laboratory studies. This system is called Global Care Quest® (http://gcq.ucla.edu/index_pc.html); it enables wireless access to all data via handheld personal digital assistant and/or tablet personal computers. This permits the physician to access online data from any of the monitors mentioned above, and to integrate the information and display it as an array of important data, similar to a pilot's

Figure 2. Cockpit view of an array of data obtained from the Global Care Quest information system

The data array can be customized to provide important information all at a glance. In this specific array a host of information is displayed including the working patient list, brain imaging, lung imaging, laboratory studies, EEG and brain microdialysis data.



cockpit array (Fig. 2). The cockpit array permits the physician to integrate and compare data that are time-locked and to begin to interrogate the data to best plan the next step of therapy.

The second approach that we have undertaken is to have remote access to the intensive-care unit (ICU). Some centers have made use of the concept of an electronic intensive care unit, which permits a clinician to view a series of monitors for a variety of patients. The electronic ICU has been shown to be associated with decreased mortality, lower length of stay in the ICU and decreased cost. In contrast to this, we have made use of the concept of telepresence. Telepresence is the concept that the clinician can be present at the bedside in spirit if not in person, and is able to observe and respond in a lifelike fashion as if the clinician were in the room itself. Telepresence is facilitated through the use of a robot® (In Touch Health, Inc. Santa Barbara, California), which is remotely controlled via an Internet connection. The telepresence robot permits the clinician to walk from bedside to bedside, look at all available charting information, perform face-to-face discussion with patients, nurses, and families, all from a remote site (Fig. 3). The remote site can be anywhere that is connected to Internet technology. The telepresence robot can be used to augment communication and obtain

visual and behavioral information that is otherwise lost by telephonic communication. The robotic telepresence is interestingly quite easy to use and is quickly accepted by nursing staff, patients and families. The secret strength of telepresence seems to be the ability to capture visual and verbal behavioral clues that occur in face-to-face interaction that is otherwise missing in telephonic or computer-based chat-room interactions. The ability of the robot to move permits freedom to wander the intensive care unit and be animated, which further creates the ambience of actually being present.

Conclusion

In summary, several avenues of advanced brain monitoring technology have been developed over the past several years, which enable the intensivist to gain an insight into the state of brain function and metabolism that goes well beyond measuring intracranial pressure. New technology is currently being developed under test conditions, which will further facilitate the integration of such technology by physicians, even if the physician is in a remote location. Indeed, this is an exciting time for the treatment of brain injury and other critical illnesses in the neurointensive care unit.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

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This is an important paper that describes the potential for hyperventilation-induced brain ischemia and suggests that brain oxygen monitoring is useful to avoid excessive hyperventilation.

Figure 3. The telepresence robot is shown in our intensive care unit interacting with the bedside nurse



The nurse is able to see and speak with the doctor via the robot as well as review the electronic bedside chart and images that are displayed (to the nurse's right). The robot is mobile such that it can move up the bedside and interact similar to a live person.

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A recent paper that highlights the lack of utility of the cerebral perfusion pressure measurement.

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