Monitoring of brain function in anesthesia and intensive care

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Purpose of review

Despite its obvious importance, the brain is inconsistently the focus of monitoring in anesthesia and intensive care settings. However, there are multiple modalities available to address cerebral monitoring that when acted upon, may improve perioperative outcomes. This review addresses the various brain monitoring options that can be integrated in anesthetic and intensive care practice in order to optimize perioperative outcomes.

Recent findings

Although numerous monitoring modalities are available, the level of evidence supporting each application is somewhat limited with few of the available monitors having been subjected to large-scale randomized trials. Despite this, they each may have a potential role to play in providing information that can be integrated to optimize care.

Summary

Using a comprehensive cerebral monitoring strategy may optimize outcomes in anesthetic and intensive care.

Keywords

anesthesia, brain, intensive care, monitoring, outcome

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Introduction

Multiple modalities to monitor the brain are available to the anesthesiologist providing care for patients in the operating room and in the ICU. Despite being arguably the most important of organs, the brain is disproportionately relatively unmonitored compared to other body systems (i.e., cardiorespiratory). Furthermore, adverse cerebral outcomes remain a continued problem in patients undergoing a variety of surgical procedures [1–3]. By providing information on a range of physiologic parameters, comprehensive brain monitoring may lead to the optimization of perioperative outcomes. The early detection of impending clinical scenarios that may predispose the brain to risk may allow for timely intervention to mitigate injury. In this review, the development of a comprehensive monitoring strategy will be discussed, outlining the clinical utility of each monitor and how it can be integrated into clinical practice.

Cerebral monitoring is an evolving area of clinical medicine, presenting clinicians with an increasing number of options intended to improve cerebral outcome during surgery. Numerous depth of anesthesia monitors, multichannel electroencephalography (EEG) monitoring, motor and sensory evoked potentials (not extensively addressed in this review), jugular venous bulb saturation, direct oxygen tissue monitors and increasingly widely available cerebral oximeters, clinicians are increasingly faced with multiple options as to how and when the brain can be monitored.

Bispectral index

EEG monitoring has been available for decades yet found little widespread perioperative use until processed EEG monitors became commonplace in the operating room. These monitors integrate single-channel EEG information via proprietary algorithms providing information on depth of anesthesia. However, there has been considerable recent debate regarding the utility of the bispectral index (BIS) monitor and its role in the prevention of intraoperative awareness. Although the BIS has been used for its purported ability to reduce the risk for intraoperative awareness, the evidence supporting this is somewhat mixed. Myles *et al.* [4], in the B-Aware trial ($n = 2463$), demonstrated that the use of the BIS monitoring in patients considered at high risk for intraoperative awareness had an 82% reduction in the relative risk of awareness when a BIS target of less than 60 was used to tailor the administration of anesthesia. Recently, however, Avidan *et al.* [5] questioned the advantage of the bispectral index over other conventional monitors to reduce awareness. In their study of 2000 patients, there was no additional benefit conferred by the BIS versus using the ubiquitously available end tidal agent (ETAG) monitor targeting patients to be maintained above 0.7 monitored anaesthesia care (MAC). In their study, they

reported two confirmed cases of awareness in those randomized to the BIS versus two awareness cases in the ETAG group. However, if one considers the reported cases of possible awareness, then the BIS group actually had more overall intraoperative awareness. This introduces the concept that if purposefully keeping patients 'on the edge' of wakefulness (as defined by a threshold of 60 BIS units), one may actually be increasing the risk of awareness (as patients may transiently periodically waver above or below this threshold, if only briefly). This risk is compounded by the uncertainty related to the BIS signal response time. That is, by the time the BIS alerts one to the possibility of awareness, the patient could unknowingly have been aware for a brief period of time [6].

Even if one discounts the awareness-related utility of the BIS, there are several other potential advantages to its use. It has been demonstrated to reduce the overall anesthetic dose used and the subsequent costs and related side-effects. In doing so, it has shortened emergence times and improved early postoperative recovery [7].

BIS can also be used to guide balancing of the patient's individual anesthetic requirements with their hemodynamic milieu. For example, in cardiac surgery it can be used to titrate the balance of very complex intraoperative hemodynamics with anesthetic goals, thus allowing the independent management of hemodynamic goals from anesthetic goals [6]. For example, before the availability of the BIS, when a patient was hypertensive, additional opiate and/or hypnotic anesthetic agents were administered (beyond what would generally be considered necessary for otherwise adequate levels of anesthesia) with the intent of attempting to reduce the perceived light anesthetic state of the patient, and thus modulate the patient's blood pressure. In effect, the hypotensive side-effects of the volatile anesthetic were often used to treat the hypertensive state despite it not being related to actual real or impending wakefulness. However, with the added information that BIS provides, it appears that the hemodynamic perturbations seen during cardiac surgery often can be aptly treated with specifically targeted vasodilator, vasopressor, and/or beta-blocker therapies if the patient has an otherwise adequate anesthetic depth. Importantly, the BIS is only an adjunct for depth of anesthesia and should be combined with the ETAG and with the integration of the traditional indicators of anesthetic depth.

Using the BIS to provide optimal anesthetic levels, and in particular, the avoidance of excessive levels of anesthetic may have particular relevance in light of the emerging data that is raising concern about potential neurotoxic effects of anesthetic agents, particularly in the developing brain [8–10]. Although this effect seems to be particularly heightened in the developing brain, elderly neurons or other ischemic neurons at risk for apoptosis have also been suggested to be more susceptible to anesthesia-induced toxicity. Thus, using the BIS to titrate anesthetic agents may avoid unnecessary increases in anesthesia doses and minimize this potential neurotoxicity.

Multichannel electroencephalography

Multichannel EEG can have an important diagnostic role in the ICU. For example, it is used in the evaluation of the comatose patient or the patient with a complex seizure disorder. Its utility in the operating room is limited to very specific indications. Surface EEG monitoring has been used for cortical mapping during epilepsy surgery. Intraoperatively, it is used during cardiac surgery for deep hypothermic circulatory arrest (DHCA) during aortic reconstructive surgery [11–17]. In this setting, it can be used as a means to determine the endpoint (i.e., EEG isoelectricity, usually defined by EEG burst suppression) for brain cooling prior to the onset of circulatory arrest. Although an argument can be made for the use of single-channel EEG monitoring from the unprocessed BIS signal, single-channel monitoring may miss residual EEG activity in other regions of the brain. Ideally, cooling should be continued for at least 5–10 min beyond the onset of EEG isoelectricity in order to insure homogeneity of brain cooling [16]. There are no studies evaluating the use of cooling time versus EEG isoelectricity onset as cooling targets as a means to optimize brain outcome after DHCA.

There are clearly pros and cons to the use of EEG monitoring during cardiac surgery. The definitive advantages have never been proven as it pertains to cerebral injury monitoring, and it is clearly not without its logistical problems. The positioning of the device in the operating room, as well as the placement of the electrodes on the scalp of the patient, requires considerable advanced planning. Trained technical assistance (i.e., designated EEG technicians and electrophysiologists) in order to obtain good quality signals and to aid in the interpretation of the data are needed and often not widely available, particularly on short notice.

No reports have identified EEG monitoring as a useful means to detect intraoperative stroke. As an investigational tool, however, it has contributed to the understanding of central nervous system (CNS) physiology, particularly in the setting of cardiac surgery [18]. More recently, quantitative multichannel EEG monitoring has been used to investigate whether it can predict, or possibly be used as a correlate of more subtle CNS injury such as neurocognitive dysfunction [19]. For example, Toner *et al.* [19] reported the relationship between postoperative cognitive loss and changes in the postoperative

EEG. In a small study ($n = 62$), they demonstrated a weak correlation between the two but had reservations about the utility of such monitoring.

In a related fashion, evoked potentials, using exogenous stimuli to monitor changes in the EEG, have been used in the setting of cardiac surgery with some interesting but preliminary results. Buziashvili *et al.* [20] have investigated the correlation of the latency of P300 (i.e., the appearance of complex waves 300 ms after auditory stimulation) with postoperative cognitive dysfunction. However, widespread adoption of this modality has not occurred.

Transcranial Doppler

Transcranial Doppler (TCD) monitoring has been used in a number of surgical settings (notably neurologic and cardiac), using measures of cerebral blood flow (CBF) velocity in the middle cerebral artery (MCA) to assess the overall adequacy of CBF. In neurosurgery and neurointensive care settings, TCD has been used to evaluate the integrity of the cerebral vasculature. During carotid endarterectomy (CEA), where decisions to augment blood pressure or to insert shunts (to increase ipsilateral CBF) are made based on observing changes in CBF with the onset of carotid clamping, the symmetry of CBF is observed. However, due to other modalities such as EEG, carotid stump pressure, and real-time cerebral oximetry, this monitoring modality is only selectively used, generally dependent upon personal preference and familiarity. In the neurosurgical ICU, patients with subarachnoid hemorrhage (SAH), can be intermittently monitored for MCA blood flow velocity to identify conditions of cerebral vasospasm.

In cardiac surgery settings, TCD has largely been used as an investigation tool for research studies. It can detect and quantify embolic phenomena in the blood transiting the MCA. In a similar fashion to CEA, it has also been used to monitor the hemispheric symmetry of CBF. However, inconsistency in acquiring an uninterrupted signal, making it difficult in up to 25% of patients to obtain a reliable signal, has been cited as a reason for considering this a monitor with suboptimal user friendliness [21]. Despite this limitation, it is often used in aortic arch surgery to detect interruptions in arch vessel blood flow that can occur due to the anatomical variations and various technical surgical challenges that can occur during these procedures.

Jugular bulb saturation

Measurement of oxygen saturation within the blood of the jugular bulb ($SjvO_2$) can provide specific information on the global oxygenation state of the brain [22]. Monitoring of $SjvO_2$ has been used during neurosurgery, in neurointensive care and in cardiac surgical procedures to detect and treat global and regional cerebral hypoperfusion [22].

Traumatic brain injury and SAH account for a large number of neurointensive care admissions and is a setting where $SjvO_2$ monitoring once saw widespread use [22]. These patients can suffer additional brain damage from hypotension, hypoxia and increases in intracranial pressure (ICP); preventing these secondary insults becomes a main goal for intensive monitoring. The detection of these secondary insults using $SjvO_2$ monitoring has been extensively investigated [22]. In one trial of traumatic brain injury patients presenting with a Glasgow Coma Scale (GCS) less than 8, a doubling of mortality in patients with a single event of $SjvO_2$ less than 50% that lasted more than 10 min was documented [23]. Furthermore, besides confirming the harmful effects of cerebral desaturation, SjO_2 monitoring can be used to direct interventional therapies. For example, the degree and duration of hyperventilation therapy can be guided by measuring $SjvO_2$ changes [24].

In cardiac surgery settings, $SjvO_2$ monitoring has been used to investigate cerebral injury [25]. The use of SjO_2 monitoring to detect patients at risk of neurological insult may guide the implementation of therapeutic interventions. Indeed, studies have demonstrated that SjO_2 is quite sensitive in detecting cerebral ischemia, but these events remain silent if mixed venous oxygen saturation (SvO_2) monitoring is relied upon [26]. Patients undergoing normothermic CPB have a higher incidence of cerebral desaturation compared to patients undergoing hypothermic CPB, indicating that hypothermic CPB may have some advantages [27]. An increased incidence of $SjvO_2$ desaturation has also been seen with off-pump coronary bypass procedures compared to conventional CABG procedures, potentially highlighting a reason why the incidence of neurologic abnormalities is the same comparing these two procedures [28].

Despite the various studies that have outlined relationships between $SjvO_2$ changes and outcomes, $SjvO_2$ monitoring is infrequently performed due to logistical issues and the relative invasiveness of the technique. Its insensitivity to local (as opposed to global) changes in oxygen saturation also reduces its utility. In cardiac surgical settings, it has largely been replaced by noninvasive monitoring of oxygen saturation using cerebral oximetry. In the neurointensive care setting, direct tissue pO_2 monitoring is slowly replacing $SjvO_2$.

Direct tissue oxygen monitoring

The development of small (i.e., relatively atraumatic) oxygen electrodes has allowed the direct measurement of

brain O_2 levels. This has primarily been used in the neurocritical care setting. Despite current medical therapy in traumatic brain injury (TBI) patients, outcome remains poor with high morbidity and mortality. Therapeutic goals include preventing secondary brain injury from cerebral ischemia through the targeted management of cerebral perfusion pressure (CPP; >60 mmHg) and intracranial pressure (ICP < 20 mmHg). Recent work has shown that cerebral hypoxia can occur despite a normal ICP and CPP highlighting that many patients with severe head injury may have impaired autoregulation [29]. This has led to the increasing adoption of brain tissue O_2 (PbtO2) monitoring as an additional monitor for patients with TBI. The Licox (Integra Lifesciences) and Neurovent (Neurovent Research Inc.) multiparameter probes have been investigated for clinical use [30]. The probe is placed through a burr hold into an area of brain (usually frontal lobe), with a normal appearance on computed tomography on the side of the maximum injury [29,31,32,33•]. Most reports outline intervening when the PbtO2 is less than 20 mmHg. Treatment is aimed at addressing the cause of cerebral hypoxia through improving oxygen delivery with ICP control (<20 mmHg), maintenance of CPP (>60 mmHg), increasing FiO2, hemoglobin manipulation, and even vasodilators [31,33•]; or by decreasing oxygen demand with sedation, and the treatment of fever and seizures [31].

In the TBI population, multiple studies have shown improved neurologic outcomes and mortality in patients treated with $PbtO_2$ directed therapy compared to standard ICP–CPP therapy [29,31,33•]. Additionally, patients having a higher quantity of ischemic events, particularly if prolonged in duration, had a higher mortality [31,33•]. Patients that did not respond to treatment of decreased PbtO2 also had worse outcomes [31]. The association between adverse $PbtO_2$ events with increased mortality has also been demonstrated in the subarachnoid hemorrhage population [32]. The investigation of $PbtO_2$ is also underway in the pediatric brain injury population [34].

Cerebral oximetry

Cerebral oximetry using near-infrared spectroscopy (NIRS) has been used in perioperative settings for more than a decade. Using similar principles as pulse oximetry, it can determine the saturation of the cerebral tissue. Using multiple wavelengths of near-infrared light, the differential absorption of this light by oxygenated and deoxygenated hemoglobin determines the overall saturation of the blood (a balance of arterial and venous, in approximately a 1 : 3 ratio) present within brain tissue.

One of the initial clinical uses for cerebral oximetry was in cardiac surgery [35]. Yao *et al.* [36] reported the relationship between the degree of cerebral desaturation (defined by the integral accounting for the amount of time and degree of cerebral desaturation) and functional brain outcome (minimental status examination and other indices of frontal lobe function). They demonstrated that the more severe the degree of desaturation that the patients experienced, the more impaired their cognitive function was. Numerous other observational reports have supported the overall clinical utility of this device. However, this observational and anecdotal evidence has only relatively recently been supplanted by more rigorous randomized controlled data specifically defining the utility of cerebral oximetry [37]. Murkin *et al.* reported a trial of 200 patients using an interventional strategy to maintain the cerebral saturation signals within 75% of their baseline value [38]; a management strategy further elucidated by Denault *et al.* [38]. This interventional strategy focused on optimizing both oxygen supply and utilization in the brain. For example, following recording of the baseline reading, the investigators instituted an interventional algorithm if the patient's saturation dropped 20% from their baseline. This intervention focused on ruling out mechanical causes for desaturation (such as cannula malplacement or jugular venous impingement due to head position), and followed with strategies to optimize oxygen supply to the brain. For example, $PaCO_2$ was returned to a normal level if patients were hypocapnic. In addition, mean arterial pressure was increased as well as FiO_2. If these actions failed to normalize the saturation, and if there was significant anemia, the patients were transfused in order to improve oxygen carrying capacity. If these efforts also failed, further suppression of cerebral oxygen metabolism was instituted with the administration of additional propofol and modest cooling.

Although not powered to examine neurological outcome (i.e., stroke), the Murkin study did demonstrate a trend toward stroke reduction using an oximetry-guided interventional algorithm. More interesting, however, was that not only was there a trend toward an improvement in neurologic outcome, but also there was a reduction in major organ morbidity. With these study results, the use of these technologies may have come full circle from only examining brain perfusion (as a means to improve neurologic outcome) to the point of monitoring the brain to use it as an index organ for overall organ function [39]. As the brain is the only major organ with a predictable proximity to the skin's surface, it has the ability to be monitored by NIRS and in doing so, it may be a better way to monitor overall organ perfusion [6].

In a similar study, Slater *et al.* [40•] also studied the use of cerebral oximetry in cardiac surgery. In their study, half of their 265 patients undergoing cardiopulmonary bypass were randomized to oximetry-guided intervention, with

the previously outlined interventions utilized if cerebral saturation (rSO2) dropped below 20% of baseline. Neurocognitive testing was performed preoperatively, prior to hospital discharge, and at 3 months. An interesting finding of this study was the clear delineation of a significant cerebral desaturation value. The authors noted that an absolute value of 50% regional oxygen saturation was required before any adverse effect was observed in a patient [40•]. In fact, patients who did not demonstrate a desaturation below an absolute value of 50% did not present with significant cognitive decline. With this discovery, a cerebral desaturation score was determined for each patient. This score was calculated by the following equation: $rSO_2 = 50\%\ rSO_2 - \text{current } rSO_2\ (\%) \times \text{time (s)}$, and determined the time in which a patient spent under this critical threshold value of 50%. The analysis of these scores revealed that an rSO_2 score greater than 3000%-seconds correlated significantly with an increased risk of cognitive impairment [40•].

However, despite the evidence that cerebral desaturation correlates with cognitive decline, it was found that the incidence of cognitive decline between the intervention and control group was not present to a statistically significant degree. In fact, the occurrence of desaturation was comparable between the two groups (58 versus 61%, respectively). Although the authors suggest that this finding was due to poor compliance with the interventional protocol, this study was unable to demonstrate that the treatment of cerebral desaturation improves patient outcome [40•]. Although the study was not specifically powered to study length of hospital stay, they found a significant correlation between prolonged rSO2 desaturation and hospital stay greater than 6 days (OR 2.71, 95% C.I. 1.31–5.60, $P = 0.07$), which may also add to the data that cerebral oximetry may be a surrogate marker for overall end organ perfusion/oxygenation.

Cerebral oximetry has also been utilized in other settings including carotid endarterectomy (CEA) [41]. Several studies have demonstrated that cerebral oximetry is beneficial in detecting cerebral ischemia during CEA and provides the same level of accuracy as other monitoring methods such as transcranial Doppler sonography [42–46]. Furthermore, many researchers have been interested in determining the threshold rSO_2 during CEA that correlates with clinical evidence of cerebral ischemia. For example, Samra *et al.* [47] utilized logistic regression analysis on data acquired by 99 patients undergoing awake CEA to determine a threshold rSO_2 value that predicted neurological dysfunction. A 20% relative decrease from baseline rSO_2 was established as a threshold value for adverse events. This cutoff point was determined to have a sensitivity of 80% and a specificity of 82% [47]. Similar results were obtained in a study performed in 2003 by Hirofumi *et al.* [44], who determined that a 16–18% rSO_2 decrease from baseline, or an absolute value of 54–56%, was predictive of neurological compromise.

A recent retrospective cohort of cerebral oximetric data from 594 CEA patients, however, was assessed to evaluate the various rSO_2 threshold values previously mentioned [48]. The results of this study presented that a 20% rSO_2 decrease from baseline, although having a high specificity of 98%, had a low sensitivity of 30% in detecting neurological complications. A cutoff rSO_2 value of 11.7% less than baseline was determined as the optimal value in predicting this adverse event. This threshold provided a sensitivity of 75% and a specificity of 77% [48]. Another distinction made by this study was the importance of the duration of cerebral oxygen desaturation on the neurological outcome. That is, a significant decrease in rSO_2 may not have any adverse effect if it occurs for only a brief period of time [48]. In summary, many studies have indicated that the use of cerebral oximetry during CEA is useful in determining cerebral ischemia. If appropriate interventions are taken to prevent a drop in rSO_2 of less than 12% of baseline, the information provided by this device may significantly improve patient outcome by preventing neurological dysfunction [41].

Conclusion

Multimodal monitoring of brain function is a growing area in the perioperative setting. No single monitor provides definitive information regarding overall brain homeostasis. However, integrating the information from several monitors may provide a means by which to guide therapeutic intervention aimed at optimizing perioperative outcomes.

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References and recommended reading

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

- • of special interest
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Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 782).

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