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Use of cerebral monitoring during anaesthesia: Effect on recovery profile

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This review article examines the effect of cerebral monitoring using an EEG-based device [i.e. bispectral index (BIS), patient state analyzer (PSA), auditory evoked potential (AEP), cerebral state index (CSI), or entropy] on titration of anaesthetic, analgesic and cardiovascular drugs during surgery. In addition, articles discussing the effects of these cerebral monitoring devices on recovery profiles following general anaesthesia, postoperative side effects, and anaesthetic costs are reviewed.

Keywords: cerebral monitors; bispectral index (BIS); patient state analyzer (PSA); auditory evoked potential (AEP) and entropy; general anaesthesia; anaesthetic-sparing and recovery.

INTRODUCTION

The impact of monitoring the level of consciousness during general anaesthesia on recovery and patient outcome remains highly controversial.[1–5] The monitoring of patient's vital signs remains the most commonly used method for determining 'depth of anaesthesia' during surgery. The value of cerebral monitoring as an adjuvant to monitoring autonomic responses to noxious surgical stimuli has been questioned by many experts in the field.[1,3,5] However, recent studies suggest that use of cerebral monitoring improves early recovery after general anaesthesia involving both intravenous (IV) and volatile anaesthetic techniques because of its ability to minimize 'over dosing' with anaesthetic drugs during the maintenance period.[6–11]

Several different electroencephalographic (EEG)-based algorithms have been evaluated in an attempt to correlate EEG-derived indices and anaesthetic drug

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concentrations with clinical signs of depth of anaesthesia.[12–15] The bispectral index (BIS), patient state index (PSI), auditory evoked potential (AEP) index (AAI), and state (SE) and response (RE) entropy indices are all processed variables derived from the EEG that have been used to quantify the sedative and hypnotic effects of anaesthetic drugs on the central nervous system (CNS). The BIS, PSI, AAI, SE and RE values are dimensionless numbers that can vary from 0 to 100, with values <60 associated with 'adequate' hypnosis under general anaesthesia and values >75 are typically observed during emergence (i.e. awakening) from anaesthesia. Although the BIS, PSI, AAI, SE and RE values have been correlated with the degree of sedation produced by IV sedative-hypnotics and volatile anaesthetics, the EEG-based indices are generally less helpful in assessing the effects of opioid analgesics, ketamine and nitrous oxide on the CNS.[16–21] Many studies have also demonstrated a good correlation between these indices and quantitative clinical assessment tools for determining the level of sedation (e.g. OAA/S score).[22,23]

In contrast to the BIS, PSI and entropy monitoring devices, the AEP monitor utilizes the middle latency auditory evoked potential (MLAEP) response to a clicking sound to assess the depressant effects of anaesthetic drugs on the CNS.[13] The MLAEP values are extracted from the EEG signal using an autoregressive model with an exogenous input adaptive method from which an AAI is calculated. Analogous to studies involving the BIS, PSI, SE and RE indices, the AAI changes in a consistent and dose-dependent manner to the administration of sedative-hypnotic and volatile anaesthetics, but not opioid analgesics, ketamine or nitrous oxide. Although Gajraj et al[21] compared AEP and BIS monitoring in spontaneously breathing surgical patients, there was no 'control' group in their study. Furthermore, these investigators did not evaluate the impact of monitoring on recovery from general anaesthesia. In a study involving patients undergoing cardiac surgery, Schwender and colleagues[24] found an association between the auditory response and implicit memory. More recently, Maattanen et al[25] reported decreased desflurane consumption during spine surgery when AEP monitoring was used to guide the administration of the anaesthetic. However, early clinical studies involving the AEP monitor have found inconsistent benefits with respect to anaesthetic-sparing and meaningful outcome variables such as the PACU recovery time, discharge times, and quality of recovery compared with standard anaesthetic practice. Bruhn et al[26] recently reported that AAI (and BIS)-guided titration to specific target ranges did not result in a reduction of desflurane consumption or recovery times during minor surgery using a remifentanil-based anaesthetic technique.

The most recently introduced cerebral monitor is the M-entropy device. In contrast to the other EEG-based monitoring systems, which combine several disparate descriptors of the EEG into a single value, the entropy monitor quantifies the regularity of the EEG signal and generates both a state entropy (SE) and a response entropy (RE) value.[15] In contrast to approximate and Shannon's entropy values which are calculated in the time domain, the SE and RE values are based on specific frequency domains. Preliminary clinical studies with the entropy monitor suggest that the regularity of the EEG increases with increasing concentrations of both intravenous (e.g. propofol) and volatile (e.g. desflurane, sevoflurane) anaesthetics.[27–32]

Despite the introduction of several different cerebral monitoring technologies, there is still no universally accepted 'gold standard' for measuring depth of anaesthesia or level of consciousness during anaesthesia.[2–5] For a monitor of anaesthetic depth to be clinically useful, it should display a strong correlation between the observed variable (e.g. BIS, PSI, AAI, SE and RE) and the patient's state of consciousness and/or physiologic responses (e.g. blood pressure, heart rate, catecholamines) to noxious stimuli during surgery independent of the anaesthetic techniques, with minimal interpatient variability. In their editorial, Kalkman and Drummond[5] argued that these conditions have not yet been achieved with any of the currently available monitoring devices.

Clinical utility studies involving cerebral monitoring with the BIS, PSA and AEP devices have demonstrated improved titration of both IV[6,9,16] and inhalation (volatile)[7,8,10,11] anaesthetics, and suggest that these devices may be useful in expediting the early recovery process. In a recently published study, Chen et al[17] and White et al[18] found a very similar pattern of changes in the BIS and PSI values during general anaesthesia involving propofol and desflurane. Similarly, the changes in the SE and RE values during general anaesthesia were also found to parallel the changes in the BIS values.[33] Of interest, both the PSI and entropy signals tend to be less suceptable to the effect of the electrosurgical unit than the BIS. Struys et al[14] reported that the BIS and AAI indices were also similar with respect to their ability to track levels of sedation and loss of consciousness with propofol. However, these investigators reported that both of these indices had poor predictive power with respect to movement in response to noxious stimuli. Schraag and colleagues[34] found that the AAI actually possessed better discriminatory power than the BIS in describing the transition from the conscious to the unconscious state. Bruhn et al[35] reported that the onset of EEG burst suppression is more accurately detected as 'deepening of anaesthesia' using the entropy (vs. BIS) monitor.

Studies have demonstrated that all of the available cerebral monitors are able to distinguish between the awake and anaesthetized states. Even though the AAI (and to a lesser degree the SE) values are consistently lower than the BIS, PSI and RE values during the maintenance period, positive correlations have been found between these indices, suggesting that all of the EEG-based monitors respond in a similar fashion to changes in the level of hypnosis. In examining the correlations between the various indices and the end-tidal volatile anaesthetic concentrations during and immediately after surgery suggests that these indices are not able to precisely quantify the effects of volatile anaesthetics on the brain.[33]

Since the BIS, PSI, AEP, and entropy values are normally higher when using these cerebral monitors compared to standard practice groups, these data suggest that patients are maintained at a 'lighter' level of anaesthesia (hypnosis) when the anaesthesiologist had access to the information provided by these monitors. The availability of the information provided by cerebral monitors not only influences the anaesthesiologist's use of the volatile anaesthetics, but also the opioid analgesics and sympatholytic drugs. As a result of the apparent anaesthetic (and analgesic)-sparing effects associated with cerebral monitoring, patients in the monitored groups may be able to more rapidly achieve surrogate recovery endpoints (e.g. fast-track eligibility)[36] and satisfy PACU discharge criteria (e.g. Aldrete score of 10).[37] The BIS value at the end of anaesthesia can also be used to predict the time required to achieve fast-track eligibility.[38] Even though patients may not be fast-tracked, the length of the PACU stay and the time to discharge home (for ambulatory surgery patients) are typically reduced by 30–60 min. Recent studies have also demonstrated improvement in the patient's quality of recovery.[10,11,39] In patients undergoing cardiac surgery, BIS-guided administration of IV anaesthetics and analgesics reduced dosage requirements without increasing the risk of intraoperative awareness or stress hormone responses.[40–42]

While studies have suggested that use of cerebral monitoring can facilitate the early recovery process by improving the titration of anaesthetic and analgesic drugs during surgery[6–11,43], in instances where intraoperative use of the monitoring device did not significantly alter the titration of the anaesthetic drugs during the maintenance period, investigators have failed to find meaningful differences in the patients' recovery profile following general anaesthesia.[44–46]. Most of the earlier studies evaluating the impact of cerebral monitoring on recovery from general anaesthesia have involved surgical patient populations receiving muscle relaxants during surgery. Although titration of the volatile anaesthetic using the BIS monitor decreased emergence times of elderly patients undergoing major orthopedic joint replacement procedures[40], no difference was observed when spontaneously breathing geriatric patients underwent brief outpatient urologic procedures.[46]

Pavlin and colleagues[47] reported that the BIS monitor has 'a limited capacity to influence the duration of recovery when used to monitor unparalyzed outpatients undergoing short surgical procedures with a relatively insoluble anaesthetic such as sevoflurane'. Use of BIS monitoring for inpatient surgery had 'minor' effects on intraoperative anaesthetic use but no impact on recovery parameters.[48] The failure to find significant differences in recovery times with cerebral monitoring could be related to many factors. For example, the impact of a cerebral monitor in improving the titration of the maintenance anaesthetic will be minimized when the device is used for relatively brief surgical procedures (i.e. less than 60 minutes). If the anaesthesiologists participating in a study had previous experience using the monitoring device for titrating volatile anaesthetics, a 'learning effect' may have carried over into the study. As a result, the anaesthesiologist's previous knowledge regarding the relationship between the end-tidal concentrations of the volatile anaesthetic and the cerebral index value under similar surgical conditions would minimize the differences in the titration of the volatile agent. Finally, if the policy of the recovery facility mandates a *minimum* length of stay and/or does not permit patients who quickly satisfy the PACU discharge criteria to more rapidly advance through the recovery process (i.e. fast-tracking), one would not expect to find differences in the intermediate and late recovery times.

Since spontaneous ventilation provides significant feedback to the anaesthesiologist on the adequacy of anaesthesia, use of an LMA (or face mask) technique would minimize the beneficial effect of EEG-based monitoring in improving recovery from general anaesthesia. Of interest, continuous EEG and electromyographic (EMG) monitoring using the so-called anaesthetic brain monitor (ABM™, Datex) was initially elevated as a 'depth of anaesthesia' monitor in spontaneously breathing patients.[49] It is also well-known that EMG activity itself can falsely elevate the EEG measurements.[50] When non-paralyzed patients received sedation in an intensive care unit, use of the BIS to guide administration of midazolam exposed the patients to 'unnecessary oversedation'.[51] Thus, it would appear that in non-paralyzed, spontaneously breathing patients, the EMG-related 'contamination' of the index value can eliminate the beneficial effects of cerebral monitoring in improving the titration of the maintenance anaesthetics. Another concern in 'minimizing' the use of anaesthetic agents also relates to the possibility that patients may experience more purposeful movements during surgery (i.e. less optimal operating conditions). Further studies are clearly needed to assess the effect of these monitoring devices on the adequacy of surgical conditions in non-paralyzed patients undergoing superficial surgical procedures. In addition, the cerebral monitors need to be evaluated during sedation procedures performed outside the operating room (e.g. diagnostic procedures, ECT treatments).[52]

It has been suggested that the use of cerebral monitors to minimize the administration of anaesthetic drugs may result in increased autonomic stress responses and adverse clinical outcomes (e.g. myocardial ischemia, intraoperative awareness).[3] Previous studies have demonstrated that patient outcome is similar whether volatile anaesthetics, opioid analgesics or sympatholytic drugs were used to control acute ‘stress responses’ during general anaesthesia.[53,54] Interestingly, a recent study by Monk and colleagues[55] found that there was an apparent correlation between the length of time during anaesthesia that the BIS value was <45 and the incidence of adverse clinical outcomes in an elderly surgical population. In studies involving cerebral monitoring devices, the hemodynamic variables during the maintenance period were similar despite the fact that the monitor-guided groups receive 15–25% less volatile anaesthetic.[7,10,11,26,43] Interestingly, patients monitored with an EEG-based cerebral device are more likely to receive β-blocking and/or sympatholytic drugs.[10,11] Importantly, there have been no serious adverse outcomes after surgery, and none of the patients in any of the studies involving cerebral monitoring have reported *recall* of intraoperative events.

Finally, cost-benefit analyses would be required to determine if the routine use of these cerebral monitoring devices in clinical practice is justified.[56] Preliminary studies[40] suggest that the anaesthetic-sparing effect of BIS monitoring fails to offset the cost of the disposable BIS electrodes. In contrast to the BIS monitor, there is relatively limited clinical experience using the PSI, AAI and entropy indices to guide the administration of anaesthetic drugs during clinical practice. Additional studies with the PSA, AEP and entropy monitors in larger, more diverse surgical populations are necessary to determine the future role of these cerebral monitoring devices ‘in routine’ clinical practice.

SUMMARY

A wide variety of electroencephalographic (EEG)-based monitoring systems have been introduced to evaluate the depressant effects of anaesthetic drugs on the central nervous system. The first commercially successful device, the bispectral index (BIS) monitor, has been found to improve the titration of both volatile and intravenous anaesthetics in paralyzed surgical populations. Although different EEG algorithms have been used for cerebral monitoring, all possess similar effects on the ability of anaesthesiologists to improve titration of anaesthetic drugs during general anaesthesia. However, all of these EEG-based indices have been shown to have a disturbingly large degree of interindividual variability. One of the major differences among the various cerebral monitoring devices relates to the susceptibility of the EEG signal to interference by EMG activity and the electrocautery unit. At present, the costs of the available monitoring devices and their disposable electrodes are similar. The most recently introduced monitoring device provides the cerebral state index (CSI). This small portable EEG-based cerebral monitoring system uses standard ECG electrode pads, and it may prove to be more cost-effective for routine monitoring than the other available devices on the market.

In conclusion, the availability of the processed EEG information provided by the entropy, AEP, PSA, CSI and BIS monitors may reduce the volatile anaesthetic requirement and contribute to a faster emergence from general anaesthesia following surgery. In addition, use of these cerebral monitors may lead to an improvement in the patient's quality of recovery. However, more detailed cost-benefit analyses are needed to encourage the more widespread use of these devices in clinical practice.

Practice points

- currently available cerebral monitors are *hypnotic* rather than 'depth of anaesthesia' monitors
- all EEG-based cerebral monitors have a similar ability to improve the titration of both intravenous and volatile anaesthetics
- improved titration of propofol and volatile anaesthetics can lead to a 15–30% decrease in the anaesthetic requirement
- the anaesthetic-sparing effect of cerebral monitoring can facilitate a faster emergence from anaesthesia, thereby enhancing the ability to provide for a fast-track recovery
- the effect of cerebral monitoring in improving the early recovery process is significantly greater in paralyzed (vs. non-paralyzed) patients undergoing general anaesthesia
- use of cerebral monitoring can reduce residual side effects (e.g. drowsiness, dizziness, fatigue, nausea and vomiting), and thereby improve the patient's quality of recovery

Research agenda

- examine the role of cerebral monitoring in preventing intraoperative awareness
- determine if avoiding excessively 'deep' levels of hypnosis improves either short or long-term outcomes in the elderly and high-risk surgical populations
- evaluate the potential benefits of using cardiovascular drugs (e.g. (-blockers, ($_2$-agonists, calcium-channel blockers, adenosine) rather than opioid analgesics to control transient autonomic responses during surgery under general anaesthesia
- study integrated approaches which involve hypnotic monitors and techniques for evaluating the autonomic nervous system (e.g. heart rate variability, pulse width) and intraoperative pain responses to determine the true 'depth of anaesthesia'
- consider the use of EEG-based cerebral monitors as part of a closed-loop drug delivery system for administering hypnotic drugs during local, regional and general anaesthesia
- evaluate the cost-benefit of using cerebral monitoring during surgery from the perspective of the patient and society at large

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