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Application of electroencephalography in the management of postoperative cognitive dysfunction

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Highlights

- Maintaining anesthesia depth within specific ranges, as indicated by electroencephalography monitors, may reduce the risk of postoperative cognitive dysfunction.
- Quantitative analysis of electroencephalography data can provide insights into the characteristics of postoperative cognitive dysfunction, aiding in its early detection and diagnosis.
- Combining electroencephalography with functional magnetic resonance imaging may enhance the assessment of brain function and improve the accuracy of monitoring devices.

Abstract

Postoperative cognitive dysfunction (POCD) is a common postoperative complication in elder patients, elevating the risk of dementia, impacting patient prognosis, and adding to the socio-economic burden. Electroencephalography (EEG) enables the recording of brain electrical activity and reflects the state of consciousness. Changes in the electrogram may signal diverse pathological and physiological states. Currently, EEG and its associated monitoring devices are extensively utilized in clinical practice. This paper presents a thorough review of the use of EEG in POCD research, aiming to establish a more substantial foundation for the prediction and prevention of POCD.

Keywords: Electroencephalography, depth of anesthesia, postoperative cognitive dysfunction, postoperative neurocognitive disorder

Introduction

Postoperative cognitive dysfunction (POCD) primarily comprises delayed neurocognitive recovery within 30 days after surgery and postoperative neurocognitive dysfunction up to or beyond 12 months. It is a subset of perioperative neurocognitive disorder, a broader category that includes both cognitive decline before surgery and postoperative delirium [1, 2].

POCD is a long-term and potentially reversible neurological complication that predominantly seen in elderly patients after major surgery. It seriously impairs patients' learning ability and memory, reduces their one-year survival rate after surgery, increases the risk of dementia, and prolongs patients' hospitalization, which inevitably adds to socio-economic burden [1, 3-7]. POCD affects an estimated 12% of patients with previously unimpaired cognitive function undergoing non-cardiac surgery under anesthesia [8]. While advanced age is a key risk factor for POCD, its incidence is also high among other age groups. With the aging of society, an increasing number of patients will undergo surgical treatment, potentially leading to a rise in the incidence of POCD. Therefore, in recent years, POCD has garnered considerable attention from scholars across various disciplines.

The exact pathogenesis of POCD remains un-

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clear; however, plausible risk factors include cerebral oxygen saturation, neuroinflammation, stress response, temperature changes, genetic predispositions, residual effects of anesthesia drugs, anesthesia drug toxicity, hypoxia, reduced cerebral blood flow perfusion, and central cholinergic dysfunction [6, 9-12]. POCD may also display a link to Alzheimer's disease (AD) through mechanisms such as amyloid β-protein accumulation and neuroinflammation [10, 13, 14]. Previous research has demonstrated the significance of electroencephalography (EEG) indicators in the early diagnosis of AD and vascular cognitive impairment [15]. The quantitative analysis of EEG may be one of the potential methods for identifying biomarkers of cognitive impairment, offering insights into predicting and diagnosing POCD [16]. Exploring whether there is a correlation between perioperative EEG metrics – indicated brain functional state and POCD and whether these indicators can predict POCD is a valuable research topic.

Definition and basic principles of EEG

The electrical signals in brain primarily derived from the synchronous summation of the postsynaptic potentials of a large number of pyramidal neurons in the cerebral cortex, which is the result of collective neuronal activity. German psychiatrist Hans Berger systematically analyzed the electrical activity of the brain and introduced the term "electroencephalogram" to describe the recorded electrical potential fluctuations of the brain.

EEG amplifies and records the brain electrical signals using external scalp electrodes, yielding complex waveforms. In perioperative settings, EEG is commonly used to record spontaneous brain activity, with two most common approaches: raw EEG (rEEG) and processed EEG. rEEG records the brain electrical signals generated by postsynaptic currents within the cortical and subcortical regions of the brain. The frequency range of raw brain electrical signals spans from 0.3 to 45.0 Hz, and rEEG frequencies are subdivided into various groups based on different frequencies: delta waves (0.4-4.0 Hz), theta waves (4-8 Hz), alpha waves (8-13 Hz), beta waves (13-30 Hz), and gamma waves (30-45 Hz) [17]. Waves above alpha waves are termed fast waves, while those below alpha waves are termed slow waves. However, interpretation of complex EEG waveforms can be challenging for non-specialist anesthetists, which has led to the development of processed EEG based on cortical electrical activity, such as bispectral index (BIS) monitors, narcotrend monitors, and entropy index monitors.

Progress of EEG in POCD

Application of processed EEG in POCD research

With the widespread use of EEG monitors in clinical practice, an increasing number of anesthetists can now assess the depth of anesthesia. Research has demonstrated that monitoring the depth of anesthesia, particularly in elderly patients, facilitates quicker recovery from anesthesia and lessens the occurrence of postoperative nausea and vomiting. Currently, there is no definitive academic conclusion on whether the occurrence of POCD can be predicted by the depth of anesthesia [18-23].

BIS

Currently, BIS is the most widely used EEG monitor in clinic. The EEG data are transformed into numbers by BIS, ranging from 0 to 100, to indicate the level of brain activity inhibition. A value of 100 shows that the brain is fully awake and a value of 0 shows that the brain is completely suppressed [24]. Several studies have recommended using BIS to monitor anesthesia depth as it may lower the occurrence of POCD. Ballard et al. demonstrated that monitoring anesthesia depth with BIS during operations could effectively prevent the occurrence of POCD [25]. Similar results were found by Chan et al., where anesthesia guided by BIS reduced the incidence of POCD at 3 months post-operation [26]. Monitoring the anesthesia depth during operation can therefore be seen as a practical measure to reduce the incidence of POCD. Chen et al. asserted the effectiveness of BIS in reducing delayed neurocognitive recovery and postoperative neurocognitive impairment, regardless of patients' age [7]. A systematic review and meta-analysis of EEG on perioperative neurological dysfunction involving 4,976 patients has demonstrated that employing BIS monitoring during surgery is associated with a lower risk of POCD [27].

Whilst numerous scholars have demonstrated that using BIS to monitor depth of anesthesia can reduce the incidence of POCD, there is still no consensus on the optimal BIS range for effectively minimizing the incidence of POCD. For elderly patients undergoing abdominal surgery, Shi et al. proposed that maintaining BIS between 45 and 60 could stabilize perioperative hemodynamics, reduce the risk of early-onset POCD, shorten the awakening time from anesthesia, and improve early postoperative cognitive function [28]. An et al. held that the use of BIS monitoring could avoid deep anesthesia and thus effectively reduce the incidence of POCD [29]. However, in a study using BIS to monitor the depth of anesthesia, Yue et al. observed that the proportion of patients with abnormal Mini-Mental State Examination score in the deep anesthesia group after surgery was significantly lower than that in the light anesthesia group, suggesting that deep anesthesia causes less cognitive impairment in patients [30]. A meta-analysis by Shi et al. showed that the incidence of early POCD was lower under deep anesthesia (BIS: 30-40) compared to conventional anesthesia [6]. Nevertheless, there is still a lack of comprehensive research, and the available randomized controlled trials do not provide sufficient data to compare the incidence of POCD at postoperative 3 or 7 days. Quan et al. reported that the incidence of POCD at postoperative day 7 was significantly lower in the deep anesthesia group (BIS: 30-45) than in the light anesthesia group (BIS: 45-60) (19.2% vs. 39.6%, p=0.032), but there was no statistical difference in the incidence of POCD between the two groups at 3 months after surgery (10.3% vs. 14.6%, p=0.558) [31]. Compared with light anesthesia, deep anesthesia is associated with a lower incidence of short-term POCD and a reduced release of inflammatory cytokines in elderly patients undergoing abdominal surgery [31]. Hou et al. considered perioperative pain as a potential factor contributing to POCD and thus excluded potential bias caused by inadequate preoperative nerve block analgesia in their study. Their results showed that in elderly patients undergoing total knee replacement surgery, lighter anesthesia (BIS: 55-65) coupled with complete nerve block analgesia reduced the development of POCD, whereas patients under deep anesthesia had a higher incidence of POCD [32].

Some research has indicated a possible link between burst suppression in EEG and postoperative delirium [33]. This sheds light on our research direction for POCD. Deiner et al. found that the lengths of burst suppression and deep anesthesia state in POCD patients were shorter, indicating that burst suppression and deep anesthesia may have a protective effect on POCD [34]. Dustin et al. discovered that the POCD patients experienced a significant increase in the duration of burst suppression during surgery [35]. However, it cannot be deduced that burst suppression has a clear causal relationship with POCD. This discovery can assist the application of intraoperative rEEG to study POCD in the future. Certain researchers have explored the correlation between BIS values and biochemical markers of POCD, such as serum S100β, which is an acidic protein that binds calcium and impacts glial cell growth and memory function. Serum S100β offers a dependable reflection of brain injury with high specificity [36]. Several studies have suggested that maintaining BIS at 30-39 benefits elderly patients undergoing abdominal surgery by significantly reducing serum S100β level and mitigating brain injury, thereby reducing the incidence of POCD [30]. Other scholars have proposed the concept of 'BISawake', which is the mean value of BIS when the concentration of disoprofol effector compartment drops to 1 ug/ml after the target-controlled infusion of disoprofol is stopped. Their study found that a BIS awake of <65 postoperatively might be a predictor of some impaired cognitive functions related to word memory [37].

Narcotrend

Narcotrend is a new type of anesthesia monitoring device that uses standard EEG electrodes to acquire and evaluate real-time EEG signals from any part of the patient's head, such as raw EEG or visual EEG. Through automated analysis, it displays the depth of anesthesia or consciousness of patients. This device allows for adjustments in the dosage of anesthetics or sedatives based on the patient's specific condition, thereby enhancing the precision of anesthesia depth and improving safety and convenience [38, 39]. It divides the rEEG into six stages and 15 levels, namely A (wakefulness), B0-B2 (sedation), C0-C2 (light anesthesia), D0-D2 (general anesthesia), E0-E2 (deep anesthesia), and F0-F2 (burst suppression), using a dimensionless anesthesia depth index (Narcotrend index) ranging from 0-100 to reflect the entire process from wakefulness to deep anesthesia [6, 38]. Narcotrend outperforms BIS as it not only distinguishes consciousness states over a broad range but also monitors sudden changes in the depth of anesthesia [40]. In a study conducted by Zeng et al. on the effects of Narcotrend on POCD, they discovered that the occurrence of POCD in patients subjected to deep anesthesia was considerably lower compared to those under light anesthesia [39]. The research highlights the value of utilizing deep anesthesia to minimize the risk of POCD. Chen et al. suggested that maintaining the depth of anesthesia within a Narcotrend index of 30-39 could improve cerebral oxygen metabolism, inhibit inflammatory reactions, and reduce the incidence of POCD in elderly patients undergoing thoracoscopic lobectomy [41]. This monitoring device can accurately reflect the level of anesthesia in each stage and can be widely applied in clinical practice to reduce the occurrence of POCD.

Other EEG monitors

The Sedline EEG monitor offers an advanced analysis of raw EEG waveform and displays the patient's current state index, density spectral array, and spectral edge frequency. Compared to the BIS and Narcotrend monitors, Sedline provides more accurate assessment of the anesthesia depth by eliminating electromyographic interference to a certain extent, and it can also identify the specific type of general anesthetic in use. However, its use for predicting POCD is still inconclusive [42]. The index of consciousness (IoC) is another novel approach to depict anesthesia depth, which quantifies EEG signals into an IoC index. Research has shown that IoC monitoring is more accurate in assessing anesthesia depth compared to BIS, and its application can significantly reduce the occurrence of POCD in colorectal cancer patients [43]. The entropy index monitor collects EEG signals and frontal electromyographic data and converts them into state entropy and reaction entropy values, representing the depth of anesthesia. State entropy and reaction entropy are indicators ranging from 0 to 91 and 0 to 100, respectively, which represent the transition from complete suppression of cortical neuronal activity to wakefulness [44]. Cotae et al. concluded that utilizing entropy index-guided anesthesia in patients undergoing non-cardiac emergency surgery may decrease the occurrence of POCD when compared to standard monitoring [45]. These EEG monitors are less widely used in clinical practice compared to BIS and Narcotrend devices, and there exists limited research on their application in POCD. However, there is currently no evidence indicating the superiority of any specific EEG quantification index in monitoring the depth of anesthesia or predicting patient prognosis. Further studies are required to substantiate the effectiveness of EEG monitors in POCD research.

Application of rEEG and quantitative EEG in POCD studies

Above studies have investigated the effect of anesthesia depth on POCD by quantitative analysis of EEG data. However, there are few experiments investigating the characteristic changes in the rEEG or quantitative EEG of POCD patients.

Prediction of POCD

Some studies have suggested that the reduction of α power in older adults during surgery is related to preoperative cognitive decline, further research is needed to ascertain the link between reduced α power in the frontal lobe and POCD [4]. Nevertheless, they also acknowledged the potential application of EEG in the prevention of POCD, believing that the reduction of α power during surgery may serve as a biomarker to identify patients with possible impaired preoperative cognitive function, allowing for intervention to prevent POCD. In the study by Hao et al., it was pointed out that the γ power ratio after anesthesia was lower than that in the awake state in the non-POCD group, and in the anesthetic state, the percentage of δ power in the total power was significantly higher in the POCD group than in the non-POCD group [46]. There were differences in EEG patterns between POCD and non-POCD patients, but the reduction in α power ratio and α power may not be risk factors for the occurrence of POCD [46]. θ band activity in the EEG is one of the most sensitive indicators of perioperative brain injury, and the increase in θ power in the EEG is associated with mild cognitive impairment and dementia [47, 48]. In a study evaluating the effects of preoperative aerobic physical training (PhT) on neurophysiological function and neurovascular biomarkers in patients undergoing coronary artery bypass grafting, it was found that patients who received PhT before surgery were less likely to suffer from POCD [16]. EEG data showed that patients who received preoperative PhT had a less pronounced increase in slow wave θ activity after surgery, indicating a lower degree of intraoperative brain injury. This provides a new approach to prevent the occurrence of POCD. Another study suggested that high frequency β rhythm power was associated with POCD in patients undergoing coronary artery bypass grafting [17]. The elevated β activity in the right frontal region and the reduced power of high frequency β oscillations in the left parietal region before surgery may serve as predictive factors for cognitive decline. Evaluation of the topographic features and dynamic processes of cortical high-frequency activity patterns may help to develop individualized rehabilitation plans for patients with POCD.

Diagnosis of POCD

In the study by Zhang et al., the characteristics of quantitative EEG in POCD patients were investigated, providing new insights into the study of EEG in POCD [49]. Their study showed that the α band energy and α variability in the EEG of POCD patients were significantly lower than those of the non-POCD control group, and they were significantly correlated with the Mini-Mental State Examination, suggesting that directional EEG may have clinical significance in the detection and diagnosis of POCD.

Prospects of using Simultaneous EEG-functional MRI (fMRI) in POCD research

fMRI indirectly reflects neural activities by measuring local blood flow metabolism. However, it is constrained by the slow hemodynamic response, with changes in blood flow occurring several seconds after changes in neural activity [50]. By combining with EEG, fMRI identifies activated brain regions and links them to specific neural responses measured by EEG at specific times, providing advantages in both temporal and spatial resolution [51]. The simultaneous EEG-fMRI facilitates the study of various cognitive functions, such as language, memory, emotion, and auditory and visual perception, through a variety of cognitive tasks, making it a leading technique in cognitive research in recent years. Cichy et al. proposed that EEG-fMRI fusion has the potential for effectively revealing the spatiotemporal dynamics of human cognitive function [52]. Its future application in POCD research is promising.

Conclusion

Currently, EEG are commonly used in clinical practice to monitor the depth of anesthesia, although there is still no definitive consensus on the relationship between anesthesia depth and POCD. The amplitude and frequency of the EEG change with age, which questions the accuracy of using EEG monitoring devices to assess the depth of anesthesia in different age groups. In addition, EEG and its derived indices can be affected by various factors, including electromyographic interference, neuromuscular blocking agents, use of medical devices, pacemakers, and compound anesthesia. It is hoped that monitoring devices can be optimized to reduce the interference of these confounding factors in the future, making intraoperative EEG monitoring more accurate and generating more accurate and consistent conclusions in future research. Furthermore, studies on the alterations in the rEEG of patients with POCD are still few. Whether it is possible to intervene and treat early POCD based on the changes in the EEG characteristics is to be expected.

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