REVIEW

CURRENT OPINION

Neuromonitoring in the elderly

Susanne Koch and Claudia Spies

Purpose of review
To summarize recent recommendations on intraoperative electroencephalogram (EEG) neuromonitoring in the elderly aimed at the prevention of postoperative delirium and long-term neurocognitive decline. We discuss recent perioperative EEG investigations relating to aging and cognitive dysfunction, and their implications on intraoperative EEG neuromonitoring in elderly patients.

Recent findings
The incidence of postoperative delirium in elderly can be reduced by monitoring depth of anesthesia, using an index number (0–100) derived from processed frontal EEG readings. The recently published European Society of Anaesthesiology guideline on postoperative delirium in elderly now recommends guiding general anesthesia with such indices (Level A). However, intraoperative EEG signatures are heavily influenced by age, cognitive function, and choice of anesthetic agents. Detailed spectral EEG analysis and research on EEG-based functional connectivity provide new insights into the pathophysiology of neuronal excitability, which is seen in elderly patients with postoperative delirium.

Summary
Anesthesiologists should become acquainted with intraoperative EEG signatures and their relation to age, anesthetic agents, and the risk of postoperative cognitive complications. A working knowledge would allow an optimized and individualized provision of general anesthesia for the elderly.

Keywords
anesthesia, elderly patients, electroencephalogram, postoperative delirium

INTRODUCTION

Intraoperative electroencephalography neuromonitoring is the most feasible and straightforward approach for tracking brain activity during general anesthesia. Berger [1] has first described systematic EEG signatures during general anesthesia with phenobarbital in 1933, identifying intraoperative EEG pattern comparable with different sleep stages. However, a routine intraoperative EEG neuromonitoring during anesthesia was not feasible until the 1990s, as smaller EEG neuromonitoring devices were developed. There has been consensus that intraoperative EEG, recorded solely on the forehead of the patient and processed by a built-in EEG analysis algorithm, can aid anesthetic dosing and expedite recovery times after general anesthesia [2,3]. The processed EEG indicates depth of anesthesia by providing a single number (index: 100–90 indicates wakefulness, 40–60 refers to optimal depth of anesthesia, 20–0 refers to excessive anesthesia, including burst suppression periods and isoelectric EEG lines) [4–6]. These EEG-based neuromonitors are easy to handle, and the single index number allows for an effortless and immediate interpretation. However, these single number indices have been deemed unreliable in clinical practice, as they do not take into account the choice anesthetic agent, age of the patient, and other factors that can influence EEG readings, such as altered brain metabolism, hypocapnia or hypercapnia, etc. As different anesthetics interact with different molecular targets in the brain [7■■], anesthesiologists tend to distrust a generalized, 'one-size fits all' index. Furthermore, intraoperative EEG signatures are dependent on age, varying significantly among young children [8–10], healthy adults, and elderly patients [5,11,12].

Despite these limitations, EEG-guided general anesthesia – based on these derived indices – was able to reduce incidence of postoperative delirium and the occurrence of long-term cognitive deficits in

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KEY POINTS

- With aging of the Western world population, an increasing number of elderly patients requiring general anesthesia is at risk of developing postoperative delirium and long-term cognitive decline.
- Intraoperative, processed EEG neuromonitoring in elderly patients is recommended to avoid excessive depth of anesthesia, thereby preventing the development of postoperative delirium.
- Intraoperative burst suppression activity can be seen in the raw EEG and indicates a very deep stage of anesthesia that can trigger the development of postoperative delirium in the elderly, whereupon elderly patients have an increased risk to incur burst suppression periods during general anesthesia.
- Increased frontal alpha-band power (seen in the density spectral array in EEG neuromonitors) is the characteristic EEG signature of stable unconsciousness induced by propofol and/or ether derived volatile anesthesia, indeed elderly patients often have reduced alpha-band power.
- Reduced functional connectivity in the EEG is seen during recovery from anesthesia, as well as in postoperative delirium in the elderly.

elderly patients [13–15]. Based on these data, the European Society of Anaesthesiology recommends in their recently published 'Guideline on postoperative delirium' [16▪▪] to guide general anesthesia in elderly patients with EEG neuromonitors, so as to reduce the incidence of postoperative delirium by avoiding periods of excessive anesthesia (Level A).

Within this review, we summarize recent investigations on intraoperative EEG neuromonitoring related to the optimization of EEG-based anesthesia guidance in elderly patients and those at risk for cognitive complications. In addition, we present EEG findings related to postoperative delirium in elderly patients, providing insights to the pathophysiological background of neuronal excitability during delirium periods.

PROCESSED EEG IN ELDERLY

As the population in the Western part of the world ages, the number of elderly patients requiring general anesthesia is increasing rapidly. In elderly patients, postoperative delirium is the most frequent brain dysfunction occurring after general anesthesia, which can transition into a long-term cognitive decline and an increased mortality [17,18]. Therefore, to avoid postoperative complications and its consequences, it is critical to improve the safety of anesthesia for these patients.

The benefits of the use of intraoperative EEG-based neuromonitoring in elderly patients to reduce the incidence of postoperative cerebral dysfunctions, which has been shown in two large, randomized studies. Radtke *et al.* assessed the occurrence of postoperative delirium in 1155 elderly patients, randomized into groups with and without bispectral index (BIS)-guided anesthesia. Postoperative delirium was detected in 16.7% of the patients in the BIS-guided group, compared with 21.4% in the BIS-blinded group [14]. In addition, a very similar study from Chan *et al.* [13] could show that postoperative cognitive decline at 3 months could be reduced in the BIS-guided group (10.2%) compared with the BIS-blinded group (14.7%). A detailed EEG data analysis indicated that prolonged periods with BIS values below 20 – indicative of a high percentage of burst suppression activity in the raw EEG – are the main trigger for the occurrence of postoperative delirium [14]. The correlation between burst suppression activity and the development of postoperative delirium was also observed in a study from Fritz *et al.* [19], in which intraoperative duration of burst suppression periods was determined by visual raw EEG data analysis. Swank and Watson [20] first described burst suppression activity in the EEG in 1949. Its main feature consists of quasiperiodical bursts of bilateral high-voltage slow waves (mainly <15 Hz) separated by low-voltage ($<5\ \mu V$) or absent activity, lasting from a few seconds to minutes, and indicating a very deep level of sedation (Fig. 1). Burst suppression activity is a characteristic EEG feature of a pathological, profoundly inactivated brain, which may also occur during hypoxia, septic encephalopathy, severe hypothermia, and other pathological brain states. Cerebral metabolism during burst suppression state is maximally reduced [21]. Based on these data, it is possible that recovery from a severely suppressed brain metabolism is hindered in elderly patients, ultimately leading to the presentation of postoperative delirium. It is noteworthy that these findings are in contrast to emergence delirium in children, in which neuronal hyperexcitability – as seen by occurrence of epileptiform discharges during anesthesia induction or increased frontal connectivity during emergence of general anesthesia – has been related to agitated emergence delirium [22,23]. These striking differences in EEG activity related to delirium in elderly patients compared with children extends into its clinical presentation, in which delirious children present with crying, agitation, disorientation, and altered response to their surroundings, whereas elderly patients present primarily with a hypoactive form of delirium [24].

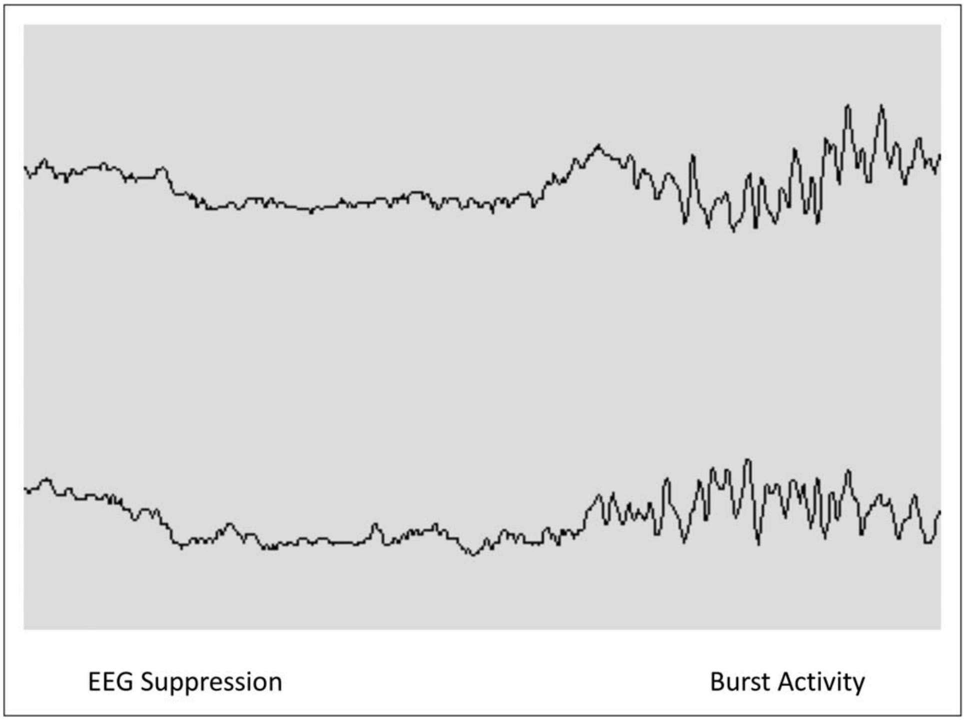

FIGURE 1. Burst suppression in raw EEG. Intraoperative raw EEG showing burst suppression activity, with a period of EEG suppression followed by an alpha-burst activity.

INTRAOPERATIVE EEG

Intraoperative frontal EEG primarily records the cortical activity of the gyrus frontalis superior (=Fp1/Fp2) and the gyrus frontalis inferior (=F7/F8). EEG recorded potentials relate to the activity of cortical pyramidal neurons, the rhythm corresponds to neuronal interactions between cortical and subcortical brain regions. Neuronal activity is influenced by cerebral metabolism, cerebral blood flow, oxygen saturation, hypocapnia/hypercapnia, glucose metabolism, and the cortical, neuronal activity itself. In addition, external artifacts, such as electric currents, muscle activity, and eyelid movement, can disturb intraoperative EEG recordings. These influencing factors must be considered during interpretation of the intraoperative EEG. Moreover, intraoperative EEG recordings display characteristic signatures related to the anesthetic agent chosen [25▪,26–28], as well as to the age of the patient and their cognitive status [5,8,9,11,12,23].

As the processed EEG indices suppose the same level of unconsciousness independently of the anesthetic agent used, age, and preexisting cognitive status of the patient, they are widely considered to be inherently inaccurate, causing distrust, and reducing the implementation of these systems in clinical routine.

ANESTHETIC AGENT-RELATED CHANGES

Anesthetics alter neuronal activity primarily by either increasing inhibition via Gamma-aminobutyric acid (GABA) GABAA receptor activation or decreasing excitation via N-methyl-D-aspartat receptor blockage, inducing neuronal hyperpolarization [7▪▪]. Due to these different mechanisms, intraoperative EEG signatures differ depending on anesthetic agent used. Below are key characteristics of the intraoperative EEG signatures of the most widely used anesthetic agents – propofol and volatile anesthetics, such as sevoflurane, desflurane.

Propofol, the most widely used anesthetic agent, binds postsynaptically at the ß-subunit of the GABAA receptor. Its binding increases not only the channel opening frequency and binding affinity for GABA, but also directly activates the receptor, even in the absence of endogenic GABA [29–31], hyperpolarizing postsynaptic neurons, thus leading to neuronal inhibition. Propofol-induced EEG signatures present in a characteristic manner related to the level of sedation [25▪,32]. EEG signatures are characterized by spectral analysis of the EEG band power, which is defined as a function of EEG wave amplitudes and frequencies. The distinct EEG frequency bands are beta 13–35 Hz, alpha 8–12 Hz, theta 4–7 Hz, delta 1–3 Hz, and infraslow less than 1 Hz band. Furthermore, EEG coherence, which can be interpreted as a measure of synchrony between two signals of the same frequency band (e.g., alpha band) in different regions of the brain, can be analyzed. During light sedation – just after administration of propofol and shortly after extubation – a period of increased beta oscillation (13–35 Hz) and reduced alpha-band power (8–12 Hz) is visible. This period is called 'paradoxical excitation' – as an increased neuronal oscillation is seen, albeit clinically accompanied by sedation and drowsiness of the patient [33]. After reaching 'loss of consciousness' through general anesthesia with propofol, infraslow (<1 Hz) and alpha-band power (8–12 Hz) increases (Fig. 2). The alpha-band power presents with a high coherent activity within the frontal cortex, in contrast to the incoherent infraslow oscillations [25▪]. In a mathematical model, this characteristic, highly coherent frontal alpha-band oscillation has been related to a thalamocortical feedback mechanism, which leads to a cortical synchrony, and induces a stable unconscious state [34,35].

Sevoflurane is an anesthetic agent with rapid induction and emergence profile. It binds at multiple targets, inducing potentiation of $GABA_A$, glycine and two-pore potassium channels, and inhibition of voltage-gated potassium channels, *N*-methyl-D-aspartate, muscarinic, nicotinic acetylcholine, and serotonin channels [7▪▪]. Similar to propofol EEG signatures, sevoflurane induces a frontal, coherent alpha oscillation and infraslow oscillations at frequencies less than 1 Hz, but in contrast to propofol, sevoflurane is also associated with an increase of coherent theta-band activity [26] (Fig. 3). The theta-band activity may be related to the modulation of T-type calcium channels in the hippocampus and in thalamic relay neurons [36]. The similarities in the alpha band are most likely related to the activation of GABAergic neural circuits, which is also seen in general anesthesia with isoflurane and desflurane [28], suggesting that these coherent alpha-band oscillations may be used as a general 'loss of consciousness' EEG signature. The coherent frontal alpha oscillation pattern limits the dimensionality of the thalamocortical network, reducing the ability of the thalamus to project and coordinate exogenous inputs to the neocortex [34].

AGE-RELATED EEG CHANGES

However, the identification of a coherent frontal alpha power may be difficult in elderly patients. Purdon *et al.* [12] examined 155 patients, aged 18–90 years of age, while receiving either propofol or sevoflurane anesthesia. With increasing age, they

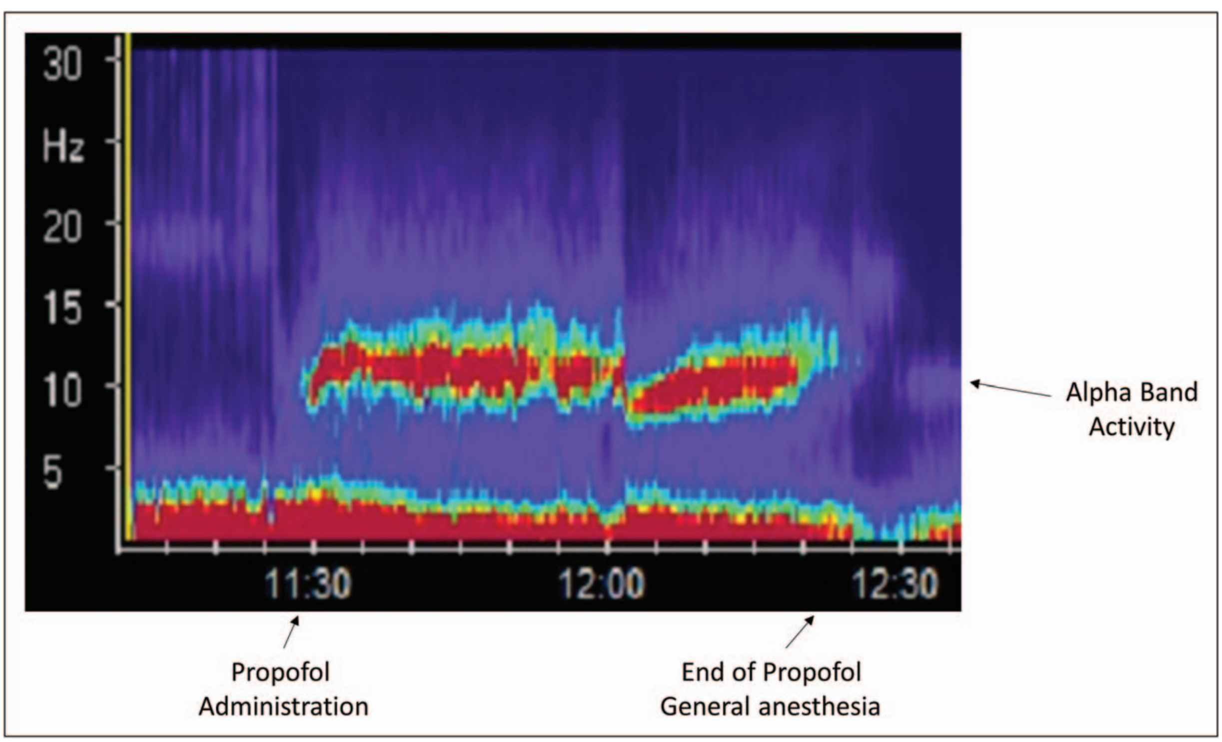

FIGURE 2. Density spectral array during propofol anesthesia. Density spectral array during propofol anesthesia. *x*-axis presents the time scale, *y*-axis the EEG frequencies (0–30 Hz), EEG power (colored scale). Propofol anesthesia starts at 11:30/ends at 12:20, demonstrating – within the period of unconsciousness – a high power in the alpha band (8–12 Hz) and within the slow-wave band (0.5–1.5 Hz).

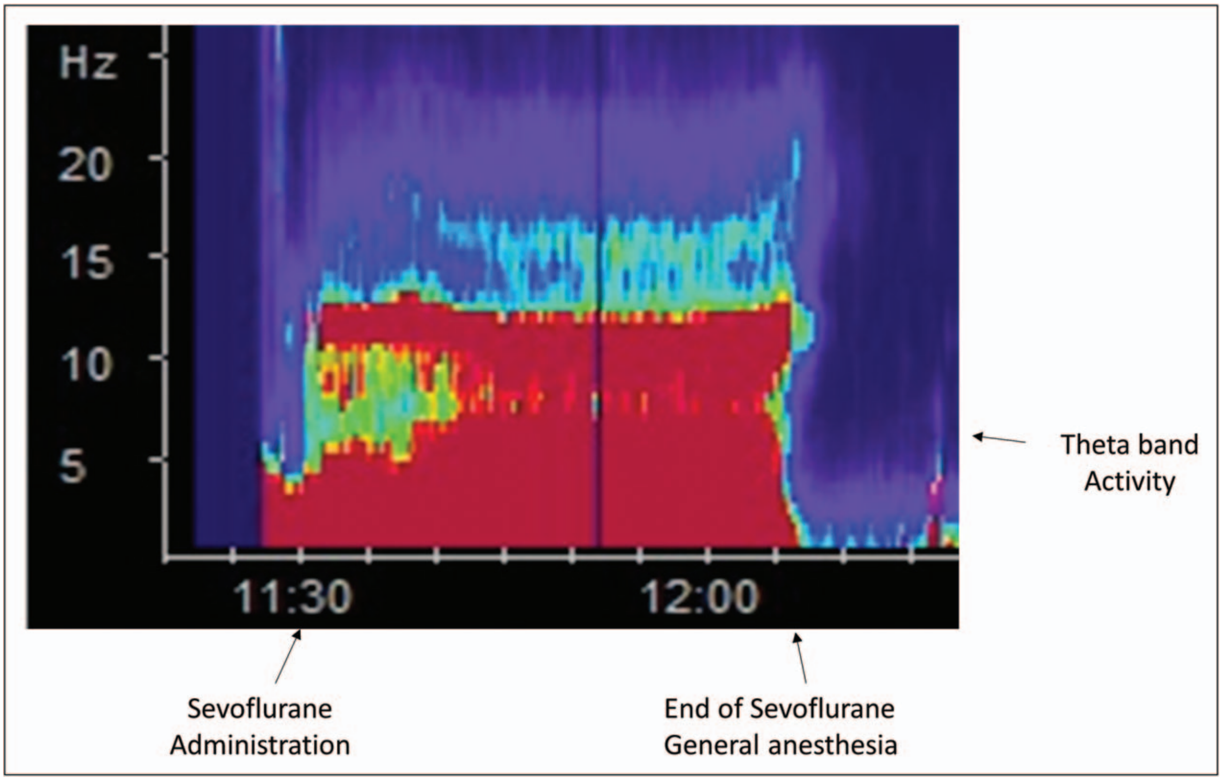

FIGURE 3. Density spectral array during sevoflurane anesthesia. Density spectral array during sevoflurane anesthesia. *x*-axis presents the time scale, *y*-axis the EEG frequencies (0–30 Hz), EEG power (colored scale). Anesthesia starts with a propofol bolus application at 11:30, sevoflurane administration starts at 11:38/ends at 12:10; demonstrating – within the period of unconsiousness during sevoflurane anesthesia besides high power in the alpha band (8–12 Hz), slow wave band (0.5–1.5 Hz), additionally high power in the theta band (3–7 Hz).

found a marked reduction in EEG signal power for all frequency bands, whereas this effect was most pronounced in the alpha-frequency band. In addition, when compared with younger patients, a loss of alpha-band coherence was observed in the elderly. They proposed that the age-related EEG power reduction might be caused by a decline in synaptic density and changes in dendritic dynamics, so that these changes might reflect functional alterations in the GABA-dependent frontal thalamocortical circuits.

Furthermore, Purdon *et al.* [12] could show that, compared with younger patients, elderly patients are more likely to experience burst suppression periods during general anesthesia. This finding is important, as duration of burst suppression during anesthesia correlates with the development of postoperative delirium in elderly patients [14,19].

Currently, all available EEG neuromonitors offer a ‘Density spectral array’ (Figs. 2 and 3), which enables anesthesiologist to guide general anesthesia in patients by observing the raw EEG activity and the frontal alpha band induced by propofol and/or volatile anesthetics. To increase the visibility of the frontal coherent alpha band in elderly patients during general anesthesia, it may be helpful to adjust the power sensitivity on EEG neuromonitors (e.g., from 15 to 30 μV) (Fig. 4). We recommend this option during general anesthesia in elderly patients, as it offers a more reliable way to identify a stable, unconscious state and avoid an excessive depth of anesthesia. Burst suppression activity may be easily seen in the raw EEG (Fig. 1), which is available in all EEG neuromonitors, clearly indicating states of anesthesia that are too deep.

EEG SPECTRAL ANALYSIS AND POSTOPERATIVE DELIRIUM

Alpha-band activity in awake patients is known to be reduced in cognitively impaired patients suffering from Alzheimer disease, as well as in those with mild cognitive impairment [37]. As alpha-band activity is also related to attention and level of sedation and unconsciousness [25▪,38], alpha-band activity appears to be an important marker of cognitive function. Alteration in alpha-band power has also been observed in patients during postoperative delirium, in which patients presented a significantly reduced relative alpha-band power in parietal and occipital regions during eye-open EEG recordings

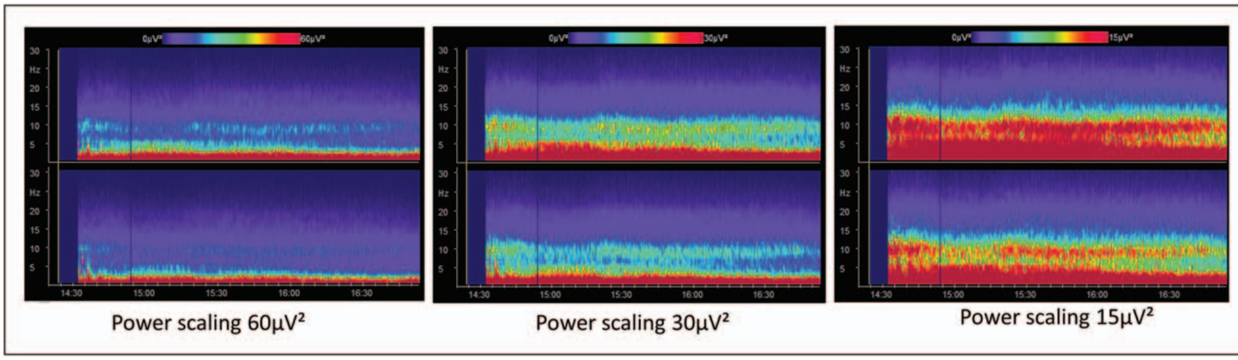

FIGURE 4. Power adaptation within the density spectral array bifrontal recording. Power adaptation within the density spectral array from 60, 30 to 15 μV^2 in a bifrontal intraoperative EEG recording during propofol anesthesia. Note the increased visibility of the alpha-band power, when changing the power scale to a higher resolution of 30 or 15 μV^2. In EEG monitors, the power scale can be changed by just select the power bar on the touch screen, which then opens up a scroll down menu.

[39]. Most recently, it has been shown that intraoperative frontal alpha-band activity correlates with reduced cognitive function in patients more than 65 years [40]. Intraoperative, frontal and parietal alpha-band power was significantly reduced in patients with lower overall cognitive abilities during general anesthesia with propofol or isoflurane. As intraoperative, frontal alpha-band activity is a signature of thalamic $GABA_A$ activation inducing a thalamocortical feedback mechanism, this suggests a critical role of cortical inhibition by $GABA_A$ activation in cognitive function in general.

EEG CONNECTIVITY AND POSTOPERATIVE DELIRIUM

It has been discussed for several years that neural synchronization is crucial for cognition, providing a means to analyze coactivation and functional connectivity. EEG connectivity refers to the synchrony and temporal correlation between two remote neurophysiological signals [41]. Directed connectivity could provide additional insights into the direction of information flow, as global organization of functional brain networks can be characterized using graph theory [42▪].

Consciousness vanishes when anesthetics induce functional disconnectivity during general anesthesia, causing loss of corticocortical information flow [43]. In elderly patients presenting with hypoactive postoperative delirium, a reduction in the alpha-band connectivity was found, similar to the disconnectivity seen in the EEG during regain of consciousness after general anesthesia [42▪]. In addition, delirious patients present with a less integrated network organization, which might reflect the inability of the delirious patient to regain organized cortical function promptly.

CONCLUSION

In conclusion, we recommend the consistent use of frontal EEG neuromonitoring during general anesthesia in elderly patients to prevent excessive depth of anesthesia and reduce the development of postoperative delirium. This approach is helpful, even when anesthesiologists guide anesthesia solely by the EEG-derived index. However, we advocate using the spectral density analysis, which is available in all commercially available EEG neuromonitors, to guide propofol and/or ether derived volatile anesthesia by focusing on the frontal alpha-band power. This easily visible alpha power band is a clear indicator of intraoperative unconsciousness. In elderly patients, it might be necessary to increase the sensitivity of EEG power presentation to better visualize the frontal alpha power band.

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Conflicts of interest

There are no conflicts of interest.

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▪▪ of outstanding interest

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