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Review

The anesthesiologist and the EEG: Current uses and future trends in the operating room

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Contents

1. Introduction

With the introduction of depth of anesthesia (DoA) monitors in ICUs and operating rooms, anesthesia providers have become comfortable relying on index numbers calculated from processed electroencephalography (pEEG) to prevent awareness and assess anesthesia depth. There are more than ten DoA monitors in the market now, with the BIS© being the most widely used. Many anesthesiologists have not been properly trained to understand the underlying processes and the limitations of the technology. They are not tapping into its full potential and may also miss or misinterpret important information. Many clinicians may rely on a number to ensure their patients' wellbeing, assuming that reading the raw EEG signal is too inaccurate or too difficult and complex to be of clinical use. There are many good articles explaining in detail how processed EEG con be interpreted [1–3]. Bottros et al. [4] showed that a training session of 45 min paired with live training enabled anesthesiologists to predict BIS numbers by looking at the raw EEG, following a study by Barnard et al. [5] and only adding more features to the training. Both studies show that the time and effort involved are manageable, and that the potential of pEEG to affect outcomes positively is not limited by what the index number says. The purpose of this review is to give a basic understanding of how EEG is recorded and processed, what information is obtainable with the current technology, and what are the future trends in its use.

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2. How is the EEG generated?

In the brain cortex, pyramidal neurons are arranged in orderly columns, with their dendritic trees extending upward and then parallel to the brain's surface. Depolarization and hyperpolarization caused by dendrite activity create potential differences between two given points on the scalp, which is what we can register. Each electrode picks changes in approximately 50–500,000 pyramidal neurons, and from other sources such as muscle activity, electrical devices in use in the room, and so on. Of all this electrical activity, the signal that we are interested in is very small, in the order of 0,5–40 μV, while the nominal voltage of a regular AAA battery is 1.5 V, and an outlet will give 120 V in North America and 220 V across Europe. This means that the technical quality of the recording is going to be very important.

On top of this, the recorded activity is influenced by what is happening in other areas of the brain, such as the rhythmic activity of the thalamus and the brainstem. These structures are involved in neuronal circuit loops with a role in maintaining level of consciousness. There is ongoing research about the exact role of the thalamus and the cortico-subcortical pathways crucial to consciousness, nociception and memory formation, and how anesthetic drugs interact with these pathways [6–11].

2.1. Recording the EEG

Typical diagnostic EEG montages follow the 10/20 system, an international standardized placement that allows for uniform spacing of electrodes, independently of head circumference. Electrodes cover the activity in scalp regions known to correlate with specific areas of cerebral cortex. Four anatomic landmarks are used: the nasion, inion, and preauricular points (Fig. 1). This setting is not very practical in the operating room (OR) or intensive care unit (ICU), where the anesthesia provider may have limited access to the scalp, or transport and other management concerns may interfere with quality signal acquisition. In this environment, simplified montages such as the hairline montage are frequently used and have in fact been adopted by commercial monitors. As the frontal lobes activity can reflect consciousness level adequately, this is the standard placement for DoA monitors, although other locations such the bridge of the nose or the retroauricular area have also been used with accurate results [12,13].

2.2. Technical quality

As stated before, the conditions in which we record the EEG can affect the reliability of the signal. The skin should be cleaned and prepped with an adequate alcohol-containing solution. Failing to do so will result in poor transmission of electricity (conductance) creating difficulties (high impedance) for good signal acquisition. This results in inaccurately high frequencies, or visible artifacts (such as a 50–60 Hz artifact where the monitor is picking electrical signals from other devices and the electrical wiring of the room). Any movement or muscle spasm (such as from a nearby Train of Four monitor) will also produce high frequency waves. Use of electrocautery will show as a cluster of spikes, and the monitor will record them as high frequency, high amplitude waves; this can be helped (but usually not completely avoided) by placing the ground plate as far from the head as possible. Finally, artifact caused by heartbeat can be identified because it is a rhythmic spike that correlates with the electrocardiogram (Fig. 2).

2.3. Interpreting what we see

A raw EEG recording can provide information about brain structure, function and relationships across different areas. Some of this can be ascertained by looking at the raw signal. To obtain more detailed information, and be able to interpret it, complex mathematical algorithms such as (but not only) the Fast Fourier transform (FFT), are applied to separate the signal into simplified components. Analyzing the frequency and amplitude of the EEG, we can identify five bandwidths (Figs. 3–1). When we talk about the "frequency domain", we are looking at the relative proportions of each bandwidth within the raw signal, while the "time domain" would be looking at how the signal changes over time. This "time domain" depicts the raw EEG signal, so patterns that are specific to some clinical conditions can be identified at first glance. This would be the case of the decrease in frequency and amplitude secondary to ischemia, the spikes in epileptic activity, or the burst suppression pattern that reflects minimal brain activity. As the EEG reflects the activity of the brain with a very short time lag, it is important to remember that sudden changes do not necessarily mean that there is irreversible damage, or that its extent can be quantified accurately.

Commercial monitors will use amplitude and frequency analysis and apply subsequent, different algorithms (most of which, such as the BIS one, are not available to the public) to give an "index", a

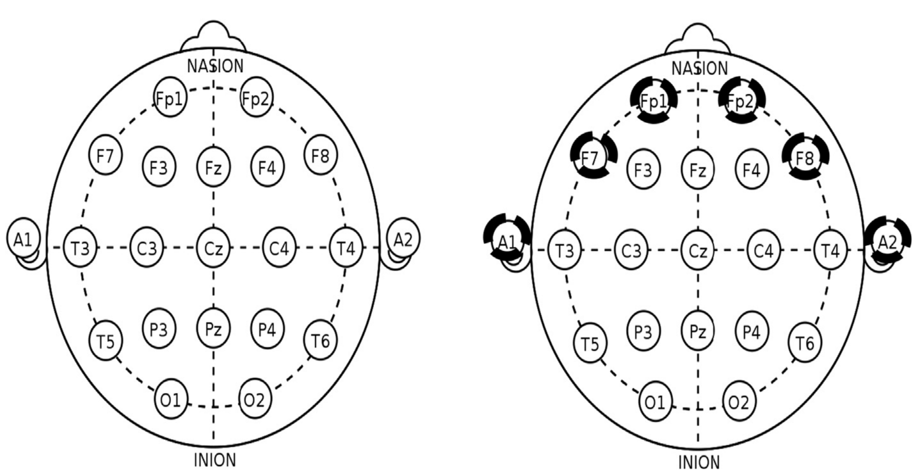

Fig. 1. 10/20 system and hairline montage. Public domain image from Wikimedia Commons (2011a).

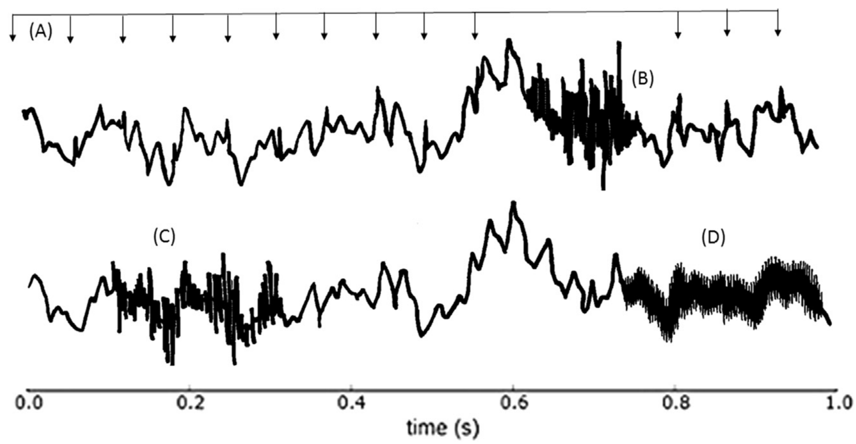

Fig. 2. Artifacts. (A) ECG spikes. (B) Electrical cautery. (C) Movement (D) 50–60 Hz artifact.

dimensionless value that correlates with level of consciousness. Monitors used in research can also analyze the synchrony of the signal across different areas of the brain, providing interesting information about neuronal pathway function (and dysfunction); and how drugs, disease, temperature, glycemia, and other factors may affect them. For a summary of the most frequently used ones and its characteristics, see Table 1.

When we analyze the EEG, we can obtain the proportion of each frequency as well as the suppression ratio (SR) that reflects how much of the brain is at a state of minimum activity (Table 2). Frequency ratios can also be plotted in a spectrogram (Figs. 3–2), for a given moment in time. We can obtain subsequent spectrograms and present them in time as a frequency over time graphic where hotter colors identify the bandwidths with more power or energy, that is, the ones in higher proportion (Figs. 3–2,3). This is called density spectral array or DSA, and it is interesting to note that different anesthetics produce different DSAs, reflecting the fact that their mechanism of action varies [8,10,14].

Being able to both see the raw signal and the resulting DSA provides a much broader understanding of what is happening in the brain than just relying on the index number alone. Besides, as the algorithms are proprietary, we don't have tools to evaluate how the components of the EEG are analyzed. This means that we don't really know what the index means, and how it is affected by what we do. There are indeed a number of case reports describing situations in which the index number was not consistent with the actual neurologic status of the patient [15–18].

Fig. 4 illustrates two such cases from our own center. In the first one, a thoracic surgery patient, there is a heavy EMG artifact (Figs. 4–1), that was eliminated through the use of neuromuscular blocking agents (Figs. 4–2). Considering only the index number would have been misleading. In another case (Figs. 4–3), a patient in ICU with severe pulmonary distress syndrome would have been under heavy sedation, because there were several electrical artifacts produced by other devices, which were being picked up by the monitor *(see supplemental electronic material).*

2.4. Depth of anesthesia vs adequacy of anesthesia

The main use of this technology has been the monitoring of anesthesia depth. Awareness during surgery happens and may have traumatic consequences [19,20]. By trusting the index number, many providers are at ease, thinking that the level of anesthesia is deep enough. This approach has two caveats: first, recall requires both cortical and subcortical activity to be present, and the latter does not seem to be adequately taken into account by the algorithms used by commercial monitors, as mentioned earlier. Second, there are other factors that influence brain activity such as age, physiologic state, temperature, and use of other drugs; what is adequate for a patient might be too much (or to little) for another. Being able to visually assess the EEG and to see the DSA can help tailor the anesthetic or sedative goals to each individual patient's needs.

Knowing how commercial monitors work and what are their strengths and limitations can be of great help assessing and understanding correctly what is happening. Table 2 shows this information in the devices that are most commonly used. For more detailed information on all the devices currently available, there is an excellent review article by Fahy et al., recently published [2].

3. What can I get out of it?

3.1. Level of consciousness and anesthetic depth

There is general consensus about the fact that pEEG guided anesthesia can reduce the risk of intraoperative awareness, especially in surgical patients who might be at risk because of their physical condition (including age and neurological disorders), have had a previous experience of awareness, or in which unusually high levels of anesthetic are being required [21–24]. It is recommended that any patient receiving total intravenous anesthesia (TIVA) be monitored with any kind of pEEG available, especially if neuromuscular blockade is used [21–23,25]. For inhalational anesthesia, there is inconclusive evidence as to whether BIS-guided vs MAC-guided is of any benefit, as the BAG-RECALL studied showed in over 6000 patients [24,25].

3.2. Management of intraoperative events

EEG has been in use for a long time, especially in cardiotorathic and vascular anesthesia, as a monitor of acute brain ischemia during surgery. Typical observations include a diminished amplitude and frequency in the raw signal. In this case, having direct access to the unprocessed EEG is important, as the index numbers may be inaccurate [26] and misguide the anesthesiologist.

EEG can be used also during the surgical management of epilepsy, as is used in diagnosis and follow up, although it is more useful for the surgeon and the neurophysiologist in this setting.

There has been considerable interest in the use of pEEG to guide closed loop anesthesia systems. It has proved better induction and

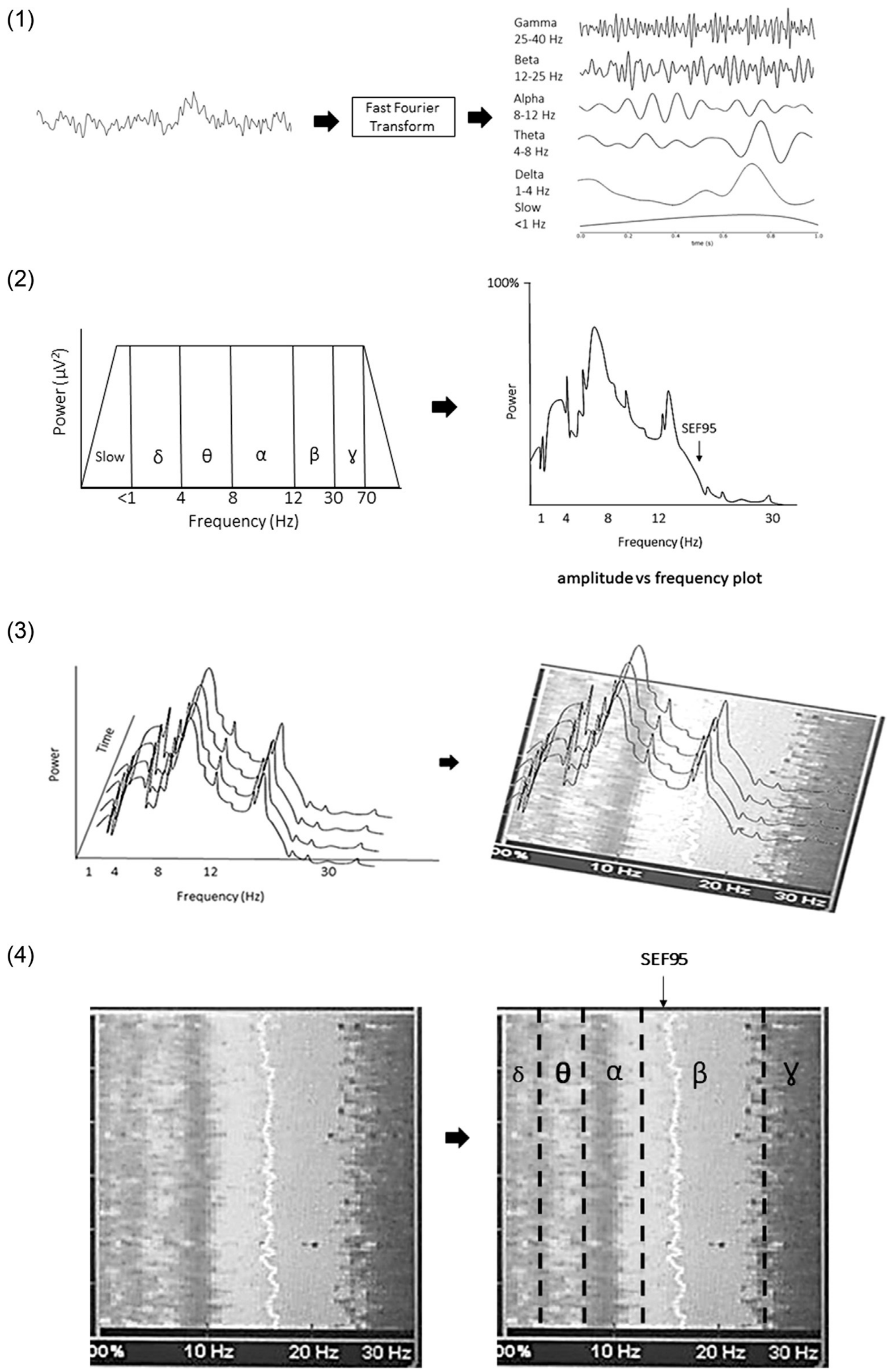

Fig. 3. Raw EEG transformation into DSA [1]. The raw signal is analyzed with Fast Fourier Transform to identify how much of the signal lies within each frequency [2]. An amplitude versus plot can then be drawn showing how power is distributed at a given point in time [3]. Superimposed over time, we obtain a 2D spectrogram in which warmer colors are assigned to the frequencies with the highest power [4]. The final DSA displayed by the monitor, with the frequency allocation.

recovery times, and use of total lower dose of propofol than manual management of perfusion pumps, especially when compared with TCI pumps [27]. However, automating anesthesia is a complex task, as there are many factors influencing anesthesia delivery; age, comorbidities, surgical events and interindividual variations in response to them and to anesthetic and adjuvant drugs all play a role in the management of successful anesthesias and surgeries [28]. Although technology is advancing rapidly, it will take some time to be able to develop algorithms capable of taking into account all these factors, and it is doubtful whether it can replace at all

Table 1
Most frequently used commercial monitors.

	BIS (Medtronic, Minneapolis, MN)	Entropy (GE Health care Technologies, Helsinki, Finland)	SEDline (PSI) (Masimo, Irvine, CA)	Narcotrend Monitor (MonitorTechnik, Bad Bramstedt, Germany)
Signal identification	Signal analysis and comparison to previous library	Signal analysis and comparison to previous library	Signal analysis and comparison to previous library	Analysis based on previous studies of algorithm response
Burst Suppression report	Yes			
Estimated time delay	15–30s	60–90s	25–30s	60–90s
Susceptible to EMG interference	Moderate	Moderate	High	Low
Capable of measuring ketamine or N2O effect	No			
Cost effectiveness	Selected high risk patients	Not enough data		
Other	Algorithm periodically updated and not disclosed to the public in its entirety. Uni or bilateral sensors available.	Reports SE (state entropy) based on EEG (index 0–91) and RE (response entropy) based on EEG and EMG (0–100)	Bilateral sensor with density spectral arrays, anterior-posterior relationships in the brain and coherence between bilateral brain regions.	Uni or bilateral. Reports 5 stages (A to F) that can be divided in further substages.

AEP: Auditory evoked potentials.

Table 2
EEG acronyms.

Acronym	Meaning	Definition	Use and example
TP	Total power	Signal power, function of amplitude (squared) microV2 (0 –20) or dB (–20 a 20).	Not of clinical interest but used to calculate other ratios.
SEF 70/90/95%	Spectral Edge Frequency	Percentage below which most of the EEG power is.	A patient under general anesthesia will typically have a SEF95 of 8–12, below the alpha bandwidth.
Bandwidth percentages	Alpha/beta/delta/theta	Relationship between frequencies among them.	A patient under general anesthesia will typically have 70–80% of the EEG on delta/theta bandwidths.
Relative power	Alpha/beta/delta/theta	Relationship between each frequency and the total power.	
SR	Suppression ratio	How much of the signal is suppressed.	

human control and management.

3.3. Nociception

There have been several attempts at developing an intraoperative pain monitor based on EEG. Most analgesic drugs act in the periphery, the spinal cord or in deep cerebral structures, while the cortex is thought to be involved in the emotional “conscious” response to pain. The complexity of the cortical response has made it difficult to develop a reliable algorithm [29]. Some recent and promising results have been published regarding an EEG derived index, the qNOX [30] but further studies are needed to validate it properly.

3.4. Prevention of delirium and postoperative cognitive disorder (POCD)

Postoperative delirium features waxing and waning mental status and changes in level of consciousness. Affecting especially older patients, it carries significant morbimortality, increasing length of stay and costs, and precluding cognitive decline very frequently. A recent systematic review estimated that up to 60% of episodes will go unrecognized, and that the real incidence is thus far higher than the reported 14% [31,32]. The cost is estimated in billions of dollars [31]. Therefore, there has been an interest in identifying EEG patterns that may put the patient at risk, such as increased time in deep anesthetic states or increased burst suppression ratio [33–35]; or that may indicate that delirium is developing or evolving [6]. Many anesthesiologists are already being careful with anesthesia depth in older adults. Other measures that have proven useful relate to management of known risk factors like post-surgical sleep impairment, immobility and functional decline, and dehydration. Agents like haloperidol or melatonin have also been used, with controversial results [36–38]. In a study over 1277 patients, anesthesiologists were randomly allocated to guide the anesthesia with and without BIS monitoring. Those who could see the number had their patients in lighter anesthesia states, and had a lower incidence of postoperative delirium, but not of cognitive decline at 3 months [39]. This reinforces the notion that POCD needs a comprehensive approach, but the pEEG can help minimize the risk.

3.5. EEG and cardiac resuscitation

There are some case reports and small series [40–42] of patients that were monitored with BIS or other forms of pEEG during cardiac resuscitation. The BIS number has not shown any correlation with neurological outcome; the SR might be an indicator that resuscitation efforts have some chance of providing a good neurological outcome. By contrast, EEG has been extensively studied *after*

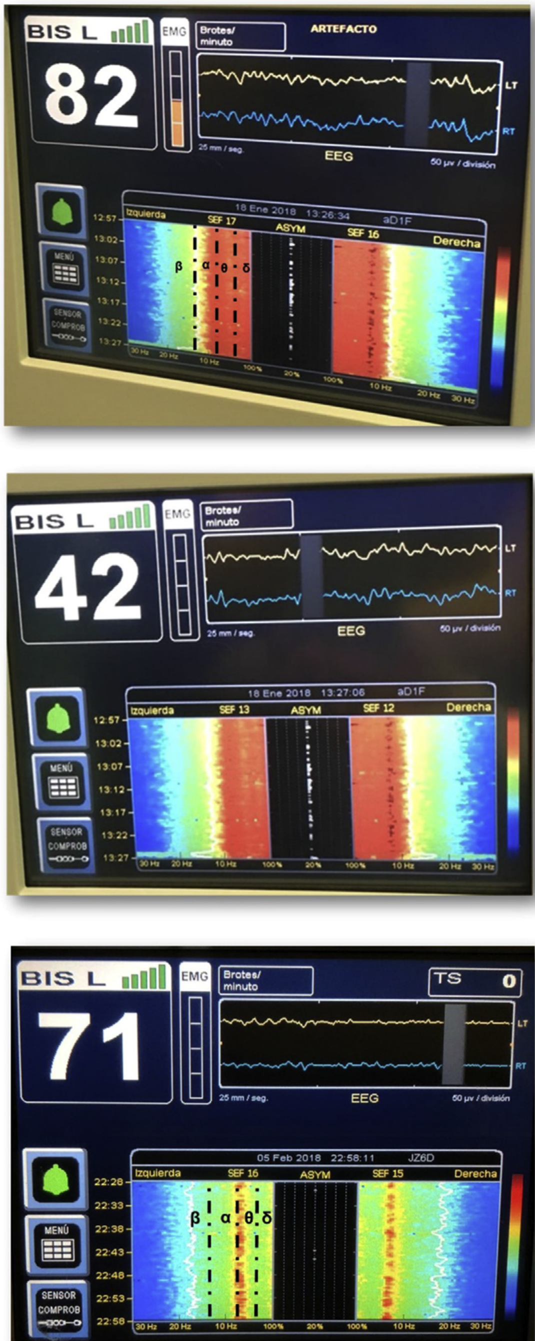

Fig. 4. Examples of absence of consistency between index number, EEG and DSA [1]. Patient underwent thoracic surgery for pulmonary lobe resection with electromyogram artifact in DoA monitor [2]. One minute later of the administration of neuromuscular blocking drugs [3]. Patient in ICU with continuous infusion of propofol, remifentanyl and cisatracurium for a severe pulmonary distress syndrome and protective mechanical ventilation with a probably artifact from any mechanical device. (1) Figs. 4–1. The index number showed a patient more nearly to awake state than under adequate general anesthesia. But EEG and DSA are consistent with a general anesthesia state. (2) Figs. 4–2. EEG and DSA were similar, but the index number had change to be consistent with the real patient's neurological status. (3) Figs. 4–3. The index number of the DoA is above the goal for general anesthesia (BIS 40–60). But EEG and DSA are consistent with general anesthesia.

resuscitation, as a tool for assessing the probability of poor neurological outcome. Once the patient is rewarmed after the initial 24 h (and it is interesting to note that both therapeutic hypothermia and a wider availability of EEG monitoring in the ICU have happened in the past 15 years), some EEG patterns have been related with poor outcome: low voltage (<20 μV) and burst suppression with identical bursts are very robust predictors [43]. A high burst suppression ratio, periodic discharges, non-convulsive status epilepticus, and nonreactive EEG among others are also related to poor outcome but its exact role has not been yet identified [44–46]. EEG should always be used in conjunction with other diagnostic and monitoring tools [47]. Recovery of normal EEG patterns within 12 h is, on the other hand, related to better outcome. Research in this field is very active and there are ongoing multicentric studies that will hopefully render some results in the near future.

4. What does the future hold?

The interest in EEG use in perioperative and critical care settings has experienced a significant increase in the last decade. As pEEG became popular because it avoided the difficulty of interpreting the raw EEG signal, anesthesiologists and critical care physicians also faced the pitfalls of not knowing exactly what the index number was providing. Recent developments in EEG processing and visualizing, such as the DSA, have made it easier to complement the index number with direct information, somehow coming full circle to looking at the raw EEG again. It has also provided new opportunities to clinical research at the bedside.

There is also an increased public awareness of the risks and consequences of intraoperative recall, due partly to better health education and partly to sensationalistic media exposure. Although the main reason for using pEEG is the better management and care of the patient, and thus their benefit, there is no doubt that DoA monitoring may become standard of care also for defensive reasons.

Lastly, there have been tremendous advances in understanding and typifying neuronal networks, their role in maintaining consciousness, and the effect of drugs and disease over them. We should expect to see refined algorithms, tailored to age, gender, pathology, and other like factors; use of Big Data and collaboration among institutions can be crucial to this endeavor. This, together with advances in technology, may allow for more refined controlled closed loop anesthesia systems, wireless bedside monitoring, or enhanced multimodal neuromonitoring in the ICU and other acute care settings. Lastly, the field of physical therapy and rehab can also benefit from the developments in understanding, analysis and applications of EEG.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tacc.2018.10.004.

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