

# Electroencephalography-based monitors

Nidhi Gupta, Gyaninder P. Singh

## Abstract

An electroencephalogram (EEG), detects changes and abnormalities in the electrical activity of the brain and thus provides a way to dynamically assess brain function. EEG may be used to diagnose and manage a number of clinical conditions such as epilepsy, convulsive and non-convulsive status epilepticus, encephalitis, barbiturate coma, brain death, etc., EEG provides a large amount of information to the anaesthesiologist for routine clinical practice as depth of anaesthesia monitors and detection of sub-clinical seizures; and also for understanding the complex mechanisms of anaesthesia-induced alteration of consciousness. In the initial years, the routine clinical applicability of EEG was hindered by the complexity of the raw EEG signal. However, with technological advancement, several EEG-derived dimensionless indices have been developed that correlate with the depth of the hypnotic component of anaesthesia and are easy to interpret. Similarly, with the development of quantitative EEG tools, the routine use of continuous EEG is ever expanding in the Intensive Care Units. This review, describe various commonly used EEG-based monitors and their clinical applicability in the field of anaesthesia and critical care.

**Key words:** Continuous electroencephalogram monitor; depth of anaesthesia monitor; electroencephalogram, monitoring, quantitative electroencephalogram monitor

## INTRODUCTION

Electroencephalography (EEG) is believed to represent a composite of the postsynaptic potentials of the pyramidal cells of the cerebral cortex. For years, it has been an invaluable diagnostic tool for neurologists in the diagnosis and management of patients with epilepsy.

Since the first observations of the effects of anaesthetic agents on EEG in the year 1937 by Gibbs *et al.*,<sup>[1]</sup> EEG has provided a huge amount of information to the

Department of Neuroanaesthesia, Indraprastha Apollo Hospitals, Sarita Vihar and Department of Neuroanaesthesiology and Critical Care, All India Institute of Medical Sciences, New Delhi, India

### Address for correspondence:

Dr. Gyaninder P. Singh, Department of Neuroanaesthesiology and Critical Care, Room No. 711, 7<sup>th</sup> Floor, Neurosciences Centre, All India Institute of Medical Sciences, New Delhi - 110 029, India.  
E-mail: drsingh\_gp@yahoo.co.in

anaesthesiologist, either for routine clinical practice as depth of anaesthesia monitors and for detection of sub-clinical seizures; or for understanding the complex mechanisms of anaesthesia-induced alteration of consciousness.

In initial years of its development, the routine clinical applicability of EEG within the anaesthesia field was hindered by the complexity of the raw EEG signal and requirement of a neurophysiologist for its interpretation. However, with technological advancement, several EEG-derived dimensionless indices have been developed that correlate with the depth of the hypnotic component of anaesthesia and are easy to interpret. Similarly, with the development of quantitative EEG (QEEG) tools, the routine use of continuous EEG (cEEG) is ever expanding in the Intensive Care Units (ICUs).

In this review, we have described various commonly used EEG-based monitors and their clinical applicability in the field of anaesthesia and critical care.

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## Raw electroencephalogram

The raw EEG is a complex random-looking waveform and has many constituent oscillations of varying amplitude and frequency. The general synchrony of the EEG appears to be related to a pacemaker-like influence from the thalamus or brainstem.<sup>[2]</sup>

The four frequently described frequency bands of the normal EEG include: Delta (0–3 Hz), theta (4–7 Hz), alpha (8–12 Hz), and beta (13–30 Hz) waves [Table 1]. A band of higher frequency is also described and is referred to as gamma waves (>30 Hz).

In general, majority of anaesthetic drugs alter the EEG by producing an initial excitatory stage characterised by desynchronisation and increased relative power of faster frequencies.<sup>[3]</sup> The fast beta ( $\beta$ ) activity is most prominent in the frontal regions and moves posterior as the anaesthetic drug effect increases. Concomitantly, a prominent area of EEG synchronisation in the alpha range (8–13 Hz) develops over the more posterior regions and moves to the frontal regions (referred to as the 'anterior topographic shift' or 'frontal dominance').

Increasing anaesthetic drug doses further causes progressive slowing until the EEG achieves burst suppression (where periods of EEG activity are interspersed with periods of a flat EEG) and finally, electrical silence or a flat EEG. Next the variability (or entropy) in the EEG decreases as the EEG becomes synchronised with the thalamic pacemaker. Finally, the electromyography (EMG) of the frontal muscles becomes quiescent as the anaesthesia deepens.

Based on these observations the EEG may be capable of reflecting a gradual change in anaesthetic effect by using a combination of EEG amplitude, frequency, variability, topography and frontal EMG.

## Processed electroencephalogram

Different methods of EEG processing have been developed to extract the EEG patterns that reflect the anaesthetic effect.<sup>[4]</sup> The general principle governing construction of EEG-derived dimensionless indices is based on the extraction of parameters from the EEG whose value is known to be statistically correlated with anaesthetic agent concentration and/or clinically assessed depth of hypnosis. With the availability of small digital computers, EEG signal processing could be accomplished by converting the analog EEG signal to a digital signal (digital domain) and using the computer to decompose the EEG into numeric components (QEEG).

The raw EEG is acquired by electrodes applied to the forehead overlying the frontal cortex, an area of the central nervous system (CNS) known to be involved in perception and memory/amenia formation. The EEG signal is then filtered and amplified, digitised and sent to the device for mathematical processing. The raw EEG is usually divided into time segments (such as 2- to 10-s periods/epoch) and processed as segments. The processing creates a normalised index, which is generally a number varying between 0 (no activity) and 100 (awake) or a letter indicating anaesthetic stage.

One of the main processing tools is Fourier transformation. This transformation is based on the Fourier theorem,

**Table 1: EEG waves and their interpretation**

| Wave                     | Frequency (Hz) | Description   | Explanation  |
|--------------------------|----------------|---|--|
| Gamma ( $\gamma$ ) waves | >30            | Higher frequency waves, markedly depressed by anaesthetics  | Are thought to play a role in perception and processing of sensory information   |
| Beta ( $\beta$ ) waves   | 13-30          | High frequency, low amplitude, awake state, usually seen in the prefrontal regions, often seen to increase during the initial stages of sedation, amnesia and anxiolysis    | Result of sensory stimuli influencing the RAS* of the brainstem which releases inhibition of the nucleus reticularis and desynchronizes the thalamic pacemakers resulting in higher frequency content in the thalamo-cortical pathways |
| Alpha ( $\alpha$ ) waves | 9-12           | Medium frequency, higher amplitude, awake but eyes closed, more prominent over the vertex   | Related to the rhythmic influence of the thalamic pacemaker cells when the inhibitory influence on the thalamus by the nucleus reticularis is reduced by meditation or anaesthesia   |
| Theta ( $\theta$ ) waves | 4-8            | Low frequency, normally seen in sleep and under general anaesthesia, normal in children, abnormal in the awake adult  | Arise from inhibition of the normal thalamic pacemaker cells by GABAergic action of the reticular nucleus  |
| Delta ( $\delta$ ) waves | 0-4            | Very low frequency, normal in infants and in stages 3 and 4 of sleep, seen in depressed functions (coma, deep anaesthesia, hypoxia, ischaemia, infarction, poor metabolism) | Delta wave with sleep spindle pattern occurs when the thalamo-cortical system is hyperpolarized, and connectivity between the environment and the brain is lost  |

\*RAS = Reticular activating system, EEG = Electroencephalogram, GABAergic = Gamma-aminobutyric acid-ergic

which essentially states that any signal can be represented by a series of sine waves of different amplitudes, frequencies and phases (the phase information describes if component waves are in synchrony with each other). Thus, a complex EEG tracing can be deconstructed and expressed as the spectrum of its component frequencies.<sup>[5]</sup>

Several other parameters can be extracted from the dissection of the EEG signal into its frequency components, and from the estimation of the relative contribution of each component (according to the frequencies and their amplitudes) to the global signal, namely the power spectrum of the EEG.<sup>[6]</sup> Examples of such parameters are the peak frequency (the one with the highest power), the median frequency (50% of power is achieved by lower frequencies, and 50% by higher ones), and the spectral edge frequency (SEF) (a specified percentage of the power is achieved by lower frequencies, generally 90% or 95%).

The SEF has been suggested to be an easily recognised parameter that follows depth of anaesthesia.<sup>[7]</sup> Trending the SEF provides easily recognised changes in SEF and quicker recognition of activation or depression of the EEG. Hence, SEF can be used as an 'early warning' indicator of impending changes in depth of anaesthesia.

The density spectral array (DSA) provides for recognition of dominant frequencies over time, displayed as increased density of data points during each epoch (2–4 s) of raw EEG analysis. The display updates over time so that one may follow changes in dominant frequencies throughout the course of an anaesthetic, surgical, or pharmacologic manipulation.

Bispectral analysis (also referred to as the bispectrum) is a mathematical technique that incorporates the phase relationships between waves by determining the phase coupling between different frequencies. This method compares different frequencies of EEG activity looking for synchrony. Deepening of anaesthesia results in increasing synchrony because of the decreasing numbers of independent pacemakers within the brain.

The burst suppression ratio (BSR) is defined as the percent time of flat line EEG in a given interval (approximately 60 s). The burst suppression pattern is easily recognised on the EEG and does not require complex proprietary algorithms to be measured. It is associated with a lower metabolic rate and may be therapeutic, or unintentionally induced as a result of high anaesthetic drug administration. Burst suppression, therefore may be a reflection of harm, therapeutic or unintentional depending on the setting.

A number of processed EEG (pEEG)-based monitors have been introduced to clinical practice. Currently available monitors with dimensionless indices include:

### Bispectral index

Bispectral index (BIS) has been the first and most studied EEG-based monitor till date. Its calculation algorithm involves power spectrum, relative activity in the  $\beta$  frequency range, burst suppression activity, synchronised fast slow activity, and bispectrum.<sup>[8]</sup>

### Entropy

Entropy measures the predictability (or the sinusoidal nature) of 2 wide EEG frequency bands: 0.8–30 Hz for state entropy (SE) and 0.8–47 Hz for response entropy (RE).<sup>[9]</sup>

SE ranges between 0 and 91 which is mainly based on cortical EEG activity, and is supposed to reflect the depth of the hypnotic component of anaesthesia. RE, in addition, takes account of facial EMG activity, which increases in case of non-counterbalanced noxious stimulation. RE ranges between 0 and 100 and its gradient with SE has been proposed to reflect the balance between nociception and anti-nociception during anaesthesia.<sup>[10]</sup>

### Patient state index

The patient state index (PSI) is derived from 4 EEG channels and takes account of the frontal localisation of power spectrum changes during anaesthesia.<sup>[11]</sup> The PSI algorithm incorporates relative activity in specific frequency bands, inter-hemispheric coherence information, as well as anteroposterior frequency and phase relationships. The output of the algorithm is a dimensionless number between 0 and 100.

### Cerebral state index

The cerebral state monitor is a battery operated handheld device that analyzes a single EEG channel and presents a cerebral state index (CSI) scaled from 0 to 100. CSI calculation involves  $\alpha$  ratio (natural log of the ratio of EEG energy in the 30–42.5 Hz band to the EEG energy in the 6–12 Hz band), the  $\beta$  ratio (natural log of the ratio of the energy in the 30–42.5 Hz band to the energy in the 11–21 Hz band), the difference between them, and the amount of burst suppression (BS%) in each 30-s period.<sup>[12]</sup>

### Narcotrend

The Narcotrend monitor analyzes stages and sub-stages of anaesthesia, and is based on similar developmental process as the BIS (although with a distinct algorithm).<sup>[13]</sup> Six different visually recognisable EEG patterns were initially identified as corresponding to different sleep stages. They were further divided into a total of 15 different patterns evidenced during anaesthesia. Each of these stages was then characterised by a set of EEG parameters, including spectrum, entropy, and autoregression. The output is a number between 0 and 100, as well as a letter corresponding to the anaesthetic stage.

### Wavelet-based anaesthetic value for central nervous system monitoring

A wavelet analysis, which captures both time and frequency domain information on the EEG signal in the form of wavelet coefficients, is used to calculate the wavelet-based anaesthetic value for CNS index, ranging from 0 to 100.<sup>[14]</sup> The reaction time of that index is shorter than the reaction time of BIS.

### SNAP index

The SNAP II is a battery operated EEG monitor that calculates a 'SNAP index' from a single channel of EEG. The index calculation is based on a spectral analysis of EEG activity in the 0–20 Hz and 80–420 Hz frequency ranges, and a burst suppression algorithm.<sup>[15]</sup> The SNAP index ranges in value from 100 to 0.

### Auditory-evoked potential index

The auditory-evoked potential index necessitates the administration of 7-Hz auditory clicks to the patient through earphones. Middle latency auditory evoked potentials are extracted from the raw EEG using a moving averaging window. The index is then calculated based on the amplitude and latency of those evoked potentials, knowing that amplitude decreases and latency increases with hypnotic depth.<sup>[16]</sup>

## INCORPORATION OF PROCESSED ELECTROENCEPHALOGRAM-BASED MONITORS INTO CLINICAL PRACTICE

### Prevention of intraoperative awareness

The incidence of awareness is believed to be between 0.1% and 0.2% in all surgical cases and is as high as 1–10% in subspecialties such as obstetric, cardiac and trauma surgery.<sup>[17]</sup> In 2012, guidelines were published by the National Institute for Health and Care Excellence in the UK recommending the use of EEG-based brain monitoring, especially in 'vulnerable' patients.<sup>[18,19]</sup>

The pEEG monitors currently available are able to discriminate awake from deeply anesthetised patients showing burst suppression with an effectiveness of over 90%.<sup>[20]</sup> However, most anaesthesiologists currently do not use these monitors either through choice or unavailability of the devices. All the more, the available large six randomised controlled trials,<sup>[21–26]</sup> undertaken until date to demonstrate any potential benefit of using these monitors for prevention of unexpected intraoperative awareness, show conflicting results.

According to Avidan and Mashour, an in-depth analysis of these studies leads to the conclusion that an EEG-driven administration of intravenous hypnotic anaesthetic agents (with pharmacological paralysis) helps prevent unexpected intraoperative awareness

with explicit recall, at least in patients at higher risk of experiencing such an event. However, when volatile anaesthetic agents are used, monitoring their end-tidal concentration, which reflects concentrations attained in the brain, and setting low concentration alarms is at least as efficient at achieving the same goal. When general anaesthesia is administered without neuromuscular blocking agents, movement might be the best indicator of awareness.<sup>[27]</sup>

Monitors that combine spontaneous pEEG indices with metrics based on evoked potentials are currently under development.<sup>[28,29]</sup> In such a monitor, analysis of spontaneous EEG signals may complement analysis of evoked EEG signals in predicting whether a patient will react to a surgical stimulus.

### Guiding anaesthetic management

EEG-based technologies may play an increasingly important role in the maintenance of general anaesthesia within the therapeutic window and tailored to the intraoperative needs of each patient. pEEG monitoring provides a combined appraisal of the CNS response to the surgical stimulation,<sup>[30]</sup> cardiovascular function, respiratory function and drug action.<sup>[31]</sup> However, to be used as effective anaesthetic titration aids, EEG monitors should allow individual drug titration, avoid episodes of over dosage, and hasten recovery when the procedure has come to its end with less side effects. Clinical studies attempting to clarify the role of pEEG monitors as anaesthetic titration aids, have given conflicting results. A meta-analysis revealed a mean reduction in anaesthetic drug consumption of 19% for BIS monitoring.<sup>[32]</sup> Ellerkmann *et al.* cited a linear correlation between the mean titrated BIS value and the hypnotic drug saving potential.<sup>[33]</sup> In contrary, pEEG monitoring did not result in significantly reduced doses of volatile anaesthetics in both the B-aware and B-unaware trials.<sup>[22,23]</sup>

In future, the refinement of 'closed-loop' systems in which anaesthetic delivery is controlled based on feedback from BIS values may aid in maintaining appropriate depth of anaesthesia.<sup>[34,35]</sup>

### As monitors of 'functional cerebral perfusion'

Both PSI and BIS seem to follow functional cerebral perfusion during periods of hypotension and resuscitation, as well as the level of hypnosis and/or depth of anaesthesia.<sup>[36–38]</sup> Clinical use of the BIS or PSI should include observations of the DSA and SEF to follow changes in underlying EEG frequencies contributing to these descriptors. Such changes need to be correlated with ongoing surgical, anaesthetic, pharmacologic, and/or physiologic manipulations.

During carotid endarterectomy (CEA) under general anaesthesia, the BIS falls and follows changes in evoked

potentials.<sup>[39]</sup> It is, however, unclear whether this is reliable as BIS has been reported a poor predictor of ischaemia in awake CEA<sup>[40,41]</sup> or outcome under general anaesthesia CEA.<sup>[42]</sup>

During periods of controlled hypotension or in trauma surgery, the appearance of elevated BSR values may indicate inadequate cerebral perfusion and alert the anaesthesiologist to an impending ischaemic event.<sup>[43]</sup> Similarly, an increase in BSR values, even at 'normal mean arterial pressure (MAP)' in elderly and chronic hypertensive patients may indicate inadequate cerebral perfusion.

### During 'pharmacological brain protection'

The BSR is used clinically to quantify the duration of flat line EEG during attempts to provide pharmacologic brain protection with propofol, barbiturates, or etomidate.<sup>[44-46]</sup> Significant theoretical reductions in CMRO<sub>2</sub> may be obtained when burst suppression is twice the duration of active EEG as approximately 60% of CMRO<sub>2</sub> is used in producing EEG. This 2:1 (suppression: burst) ratio may reduce CMRO<sub>2</sub> by 40% (2/3 of 60), provided the suppression duration is at least 10 s.<sup>[47]</sup>

### Assessing the balance between noxious stimulation and anti-nociception

BIS and EMG variability, or an index combining both parameters (the composite variability index, ranging between 0 and 100), has been proposed for assessing the adequacy of anti-nociception during anaesthesia.<sup>[48]</sup> BIS variability can be estimated using the standard deviation of BIS values recorded during the previous 3 min. EMG variability corresponds to the standard deviation of EMG power over the same period of time. The algorithm for its calculation has been designed according to the ability of sub-parameters to predict the occurrence of a somatic event (or patient movement) in response to noxious stimulation, in absence of muscle relaxation. Another EEG-derived parameter proposed to assess anti-nociception is the aforementioned RE-SE gradient of Spectral Entropy.<sup>[49]</sup>

### Optimising peri-operative outcomes

#### Effect on early recovery

Amidst conflicting study results, the role of pEEG guidance in improving early recovery outcomes remains unclear. In a meta-analysis, Liu, reported a modest reduction in anaesthetic consumption, risk of post-operative nausea and vomiting (PONV), and recovery room time in patients undergoing ambulatory anaesthesia with use of BIS monitoring.<sup>[32]</sup> Later, another Cochrane meta-analysis also found that BIS monitoring significantly reduced propofol and volatile anaesthetic consumption, early recovery times, and length of post-anaesthesia care unit (PACU) stay.<sup>[50]</sup>

However, in a large, randomised clinical trial Pavlin *et al.* reported that although BIS monitoring was associated with a slight decrease in sevoflurane administration, it did not lead to faster emergence or a shorter stay in the PACU.<sup>[51]</sup> Similarly, analyses from the BAG-RECALL and B-unaware trial populations and the Michigan Awareness Control Study demonstrated no difference in anaesthetic administration, time to discharge from the post-operative recovery area, or incidence of PONV with the use of BIS guidance compared with controls.<sup>[26,52]</sup>

#### Effect on post-operative mortality

An association has been found between prolonged time with low EEG indices during anaesthesia and poor long-term outcomes, but not with absolute amount of anaesthetic agent received.<sup>[53-56]</sup> Whether these findings are related directly to low BIS scores or reflect an intrinsic sensitivity of the brain to the effect of anaesthetic agents in vulnerable patients is not yet clear.

In 2012, Sessler *et al.* reported findings from a large observational study of the possible influence of low MAP, low BIS and low minimal alveolar concentration (MAC) on 30-day post-operative mortality.<sup>[57]</sup> Authors found that low BIS (<45) in isolation was actually associated with a decreased risk of 30-day mortality whereas, when low BIS occurred concurrently with the 'triple low' (low MAC, low MAP, or both low MAC and low MAP), there was an increased adjusted risk of 30-day mortality. Currently, large clinical trials are underway to determine whether triple low or deep anaesthesia (e.g., low BIS) do indeed contribute to negative post-operative outcomes.

### Understanding mechanisms of general anaesthesia

EEG studies, either alone or in combination with other techniques such as transcranial magnetic stimulation, have contributed to the considerable progress that has recently been made in the understanding of the mechanisms of anaesthesia-induced alteration of consciousness.<sup>[58,59]</sup> The advantage of EEG over other technique, is that it allows exploring functional effective connectivity, or causal influence, between brain regions rather than statistical dependencies in changes of indirect signs of regional brain activity.<sup>[60]</sup>

### As a diagnostic tool in patients with epilepsy

The EEG can be the most helpful test to determine a diagnosis of epilepsy. It can also distinguish focal and generalised neurophysiologic correlates of epilepsy.<sup>[61]</sup> Furthermore, when paired with video monitoring, EEG can not only define epileptic and non-epileptic events but also aid in localisation of seizures in patients with epilepsy.

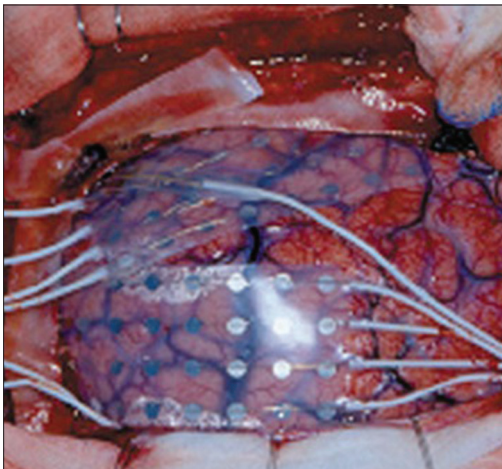
Invasive intraoperative monitoring by electrocorticography [Figure 1], after placing intracranial depth wires or

subdural grid electrodes, may be required in patients with refractory focal epilepsy with the common goal of better defining the cortical areas to be resected (ictal onset localisation) and/or to minimise the risks of post-operative unacceptable deficits by cortical mapping of functional cortex with electrical stimulation (usually speech, motor, sensory, and visual systems).<sup>[62,63]</sup>

## CONTINUOUS ELECTROENCEPHALOGRAM MONITORING IN THE INTENSIVE CARE UNIT

In the neurocritical care setting, the clinical examination is often clouded by coma, sedatives, toxic encephalopathy, or disorders of primary neurological modalities. Continuous EEG [Figure 2] provides information about brain electrical activity, even when brain function is depressed, and thus has a rapidly expanding role in the context of monitoring, early diagnoses of sub-clinical seizures and non-convulsive status epilepticus, treatment and prognostication among critically ill-patients with impaired consciousness [Table 2].<sup>[64,65]</sup>

Focal EEG slowing may indicate ischaemia, whereas global slowing is suggestive of encephalopathy. For prognostication purpose, reduced percentage of alpha variability and absent EEG reactivity may indicate severe neuronal injury and poor prognosis. The neurointensive care section of the European Society of Intensive Care Medicine recommends cEEG monitoring in patients with generalised convulsive status epilepticus and to rule out non-convulsive seizures (NCS) in brain-injured patients and in comatose ICU patients without primary brain injury who have unexplained and persistent altered consciousness. The panel also suggests EEG to detect ischaemia in comatose patients with subarachnoid haemorrhage and to improve prognostication of coma after cardiac arrest.<sup>[66]</sup>



**Figure 1:** Intraoperative monitoring by electrocorticography

In addition, EEG monitoring in ICU is also useful to help assess the depth of sedation, monitor barbiturate coma for refractory intracranial hypertension<sup>[67]</sup> and is mandatory in several countries for the diagnosis of brain death.<sup>[68]</sup> It could also be useful for the early diagnosis of acute anoxic-ischemic brain injury or intracranial hypertension cerebral damage; this type of indication is still under evaluation.<sup>[64,69]</sup>

## TECHNICAL CONSIDERATIONS

Periodic discharges (PDs) including (pseudo) periodic lateralised epileptiform discharges (PLED), bilateral independent pseudoperiodic lateralised discharges, generalised periodic epileptiform discharges, and triphasic waves (TWs) are patterns often encountered in ICU EEG.<sup>[70]</sup> Technical choices such as types of electrodes, montages, as well as parameters of quantified analysis are based on clinical indications, the patient's state of consciousness and the expected total duration of the EEG monitoring. Classic disc electrodes (Ag-AgCl) positioned on the scalp with water-based adhesive paste, or held by a mesh net or bandage, are usually recommended. Its disadvantage lies in the lengthy set-up time and the generation of artifacts if a computed tomography scan or magnetic resonance imaging becomes necessary.

Needle electrodes, faster to install and triggering less artifacts, are more invasive and must be restricted to specific situations (e.g. diagnosis of brain death, coma, limited access to the scalp).<sup>[71]</sup> A minimum of 8-electrode montage (electrode positions defined according to simple skull landmarks while respecting the 10/20 international system) is recommended, that can help detect up to 93% of epileptic seizures.<sup>[72]</sup> In addition, concomitant EEG video recording helps evaluate electro-clinical correlations of seizures and identify the origin of artifacts.

To facilitate the interpretation of cEEG, digital trend curves based on various signal characteristics can be



**Figure 2:** Continuous electroencephalography monitoring

**Table 2: Role of cEEG monitoring in the ICU**

| Medical illness   | Prevalence of seizures (%) | Importance of cEEG monitoring for |                      |           |
|---|----------------------------|-----------------------------------|----------------------|-----------|
|   |                            | Seizure detection                 | Monitoring/treatment | Prognosis |
| Intracerebral haemorrhage   | 10-30                      | ++                                | +                    | Uncertain |
| SAH   | 4-16                       | ++                                | ++ for vasospasm     | ++        |
| Traumatic brain injury  | 22-33                      | ++                                | ++                   | ++        |
| Ischemic stroke   | 5                          | +                                 | Uncertain            | +         |
| Post-cardiorespiratory arrest/<br>hypoxic-ischemic encephalopathy | 10-33                      | +++                               | +++                  | +++       |
| In medical ICU patients with<br>severe sepsis                     | 11                         | +                                 | Uncertain            | Uncertain |

Tentative grading of importance of cEEG = + = Minor importance, ++ = Moderate importance, +++ = Strong importance, cEEG = Continuous electroencephalogram, ICU = Intensive Care Unit, SAH = Subarachnoid haemorrhage

displayed synchronously with the EEG. Most common used are amplitude-integrated EEG (a-EEG) and spectral array ([DSA] or compressed spectral array [CSA]). Visualised on one sole display graph, these trend curves can facilitate the identification of very slow changes in EEG background activity and their variation (alertness cycles, changes linked to treatment administrations) as well as seizure patterns and their quantification. Spectral analysis from each hemisphere may also be compared to provide an asymmetry spectrogram to assess the difference in amplitude between cerebral hemispheres for each frequency.

In the a-EEG, EEG is compressed over time and adjusted in amplitude on a semi-logarithmic scale. Specific a-EEG devices are commonly used in the neonatal ICU.<sup>[73]</sup>

## INDICATIONS FOR CONTINUOUS ELECTROENCEPHALOGRAM MONITORING IN THE INTENSIVE CARE UNITS

### In neurocritical care patients

cEEG monitoring is useful in identifying sub-clinical seizures and NCS and guiding anti-epileptic therapy.

The diagnosis of NCS is essential in the ICU, especially in unexplained disorders of consciousness, since their presence has been correlated with a poorer prognosis and a delay in diagnosis appears to increase patient mortality.<sup>[74]</sup>

In the absence of clinical symptoms and EEG monitoring, most of the NCS would go unrecognized as differentiating ongoing seizure activity from postictal or medication-induced encephalopathy can be quite challenging in comatose ICU patients. In patients with acute neurological diseases, NCS were detected in 21% of patients.<sup>[75]</sup> Among these patients, EEG diagnosis of NCS was preceded by clinical seizures only in 25% of cases, whereas subtle clinical findings, such as oral or ocular

muscular movements and/or gaze deviation, were found in 50%.<sup>[75]</sup> cEEG is recommended over intermittent EEG because of the intermittent nature of occult seizures.<sup>[66]</sup> Using cEEG recording, 56% of seizures are detected in the 1<sup>st</sup> h, and 88% in the first 24 h.<sup>[76]</sup>

cEEG also helps guide status epilepticus treatment, especially in case of refractory status epilepticus treated by deep sedation by anaesthetic agents.<sup>[77]</sup>

### In critically ill-patients with primary non-neurological illness

EEG monitoring is required for early diagnosis of NCS and improves coma prognostication after critical illness and cardiac arrest. NCS and PD are common in patients with severe sepsis and altered mental status, and are associated with poor functional outcome.<sup>[69]</sup> However, a lack of EEG reactivity was found to be associated with higher 1-year mortality than the presence of PD or NCS (mean survival time 3.3 [95% CI: 1.8–4.9] vs. 7.5 [6.4–8.7] months;  $P = 0.002$ ) in patients with severe sepsis.<sup>[65]</sup>

After cardiac arrest, post-anoxic encephalopathy needs to be differentiated from status epilepticus. EEG is required as most seizures after cardiac arrest are non-convulsive and to differentiate myoclonic status epilepticus from peripheral or subcortical myoclonus.<sup>[78]</sup> In addition, hypothermia and sedation used during cooling alter motor response and decrease the prognostic accuracy of neurological examination.

EEG can reveal different type of abnormalities: Burst-suppression, spikes, spikes-and-waves, polyspikes-and-waves, diffuse polyspikes or TWs, often periodic or pseudoperiodic. The presence of discontinuous and burst-suppression pattern and of non-reactive EEG background were found to be strongly correlated with a poor prognosis, while a continuous reactive background was associated with good recovery.<sup>[79,80]</sup>

Other automatic approaches using EEG-based evaluation of auditory functions, the so-called mismatch negativity – an automatic fronto-central EEG component occurring at 100–150 ms after the onset of a sound deviation has also been tested for prognostication. One study showed that an intact auditory processing was present even in comatose patients with extended brain damage after cardiac arrest, whereas a deterioration of auditory discrimination over time was highly predictive of poor outcome.<sup>[81]</sup>

### To detect cerebral ischaemia

EEG has become widely adopted for the detection of SAH-related vasospasm. Preliminary studies have demonstrated that cEEG may become a potential useful tool in the monitoring of cerebral vasospasm, allowing rapid diagnosis (24–48 h prior to other diagnostic tools) and therapy before irreversible brain damage occurs.<sup>[82-84]</sup> In these studies, quantitative cEEG variables such as changes in total power, relative alpha variability, the alpha/delta ratio and novel variable measuring alpha power and variability, termed composite alpha index have been evaluated as sensitive predictors of the development of vasospasm. An advantage of cEEG over other monitors of cerebral vasospasm (e.g., transcranial Doppler ultrasonography and cerebral angiography) is that it can be monitored continuously allowing an early therapy.

In acute ischaemic stroke, QEEG provides a good assessment of stroke size and severity.<sup>[85,86]</sup> In patients with haemorrhagic stroke, PLEDs are often observed in cortical haemorrhages and are correlated with a poorer prognosis.<sup>[87]</sup>

### To monitor barbiturate coma for refractory intracranial hypertension

An additional role for EEG in guiding therapy is in the management of refractory intracranial hypertension. Although still controversial, due to the effects of hypotension and infection,<sup>[88]</sup> barbiturate sedation should be performed in conjunction with EEG to minimise the amount of medication by treating only until burst suppression has been obtained. Despite being a common practice in the ICU, the duration of such suppression has yet not been determined.

### Limitations of electroencephalogram-based monitors

The accurate interpretation of EEG-derived indices is limited by several confounding factors, which may lead to erroneous conclusions. They include inter-individual variability in terms of baseline EEG characteristics,<sup>[89]</sup> erroneous site of EEG recording, artifacts from surrounding electrical devices (electrocautery, pacemakers, warming devices, EMG),<sup>[90-92]</sup> and specific clinical conditions such as hypothermia, hypoglycaemia,

dementia, cortical atrophy, advanced age, seizures and cerebral ischaemia.<sup>[40,93-96]</sup> Several studies have reported that BIS values are less reliable in infants and small children.<sup>[97,98]</sup> Ketamine and nitrous oxide tend to increase the BIS score and increase depth of anaesthesia.<sup>[99,100]</sup> BIS values have been shown to decrease in patients receiving neuromuscular blockers, both while fully conscious<sup>[101]</sup> or while anaesthetised.<sup>[102]</sup>

Acquisition and interpretation of cEEG in ICU is limited by a number of factors including wounds or bandages (that limit EEG electrode placement), sweating, muscle activity, and movements commonly seen in delirious or agitated patients. Electrical interference may occur from mechanical ventilators, machines for renal replacement therapy, neuromonitoring apparatus, pumps, and electronic beds.

## CONCLUSION

EEG provides a large amount of information to the anaesthesiologist, both for routine clinical practice and for the understanding of the mechanisms of anaesthesia. Incorporating pEEG monitors into routine anaesthetic practice can improve anaesthetic management and patient outcomes by optimising the depth of anaesthesia. However, all interpretations of monitored parameters require inspection and consideration of potential artifacts prior to any clinical decision-making. In future, advances in EEG analysis may provide the means to develop specific monitors of cortical connectivity, and particularly of fronto-parietal feedback connectivity, which is thought to be a sign of consciousness.

In ICU settings, cEEG can convey a tremendous amount of physiologic information and has the power to detect both ictal and inter-ictal EEG patterns. Future clinical trials using cEEG and other real-time, continuous monitors (non-invasive or invasive) will be useful and crucial to understand primary brain dysfunction as well as to reduce the risk of secondary brain injury in susceptible critically ill-patients.

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