Practical Use of the Raw Electroencephalogram Waveform During General Anesthesia: The Art and Science

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Quantitative electroencephalogram (qEEG) monitors are often used to estimate depth of anesthesia and intraoperative recall during general anesthesia. As with any monitor, the processed numerical output is often misleading and has to be interpreted within a clinical context. For the safe clinical use of these monitors, a clear mental picture of the expected raw electroencephalogram (EEG) patterns, as well as a knowledge of the common EEG artifacts, is absolutely necessary. This has provided the motivation to write this tutorial. We describe, and give examples of, the typical EEG features of adequate general anesthesia, effects of noxious stimulation, and adjunctive drugs. Artifacts are commonly encountered and may be classified as arising from outside the head, from the head but outside the brain (commonly frontal electromyogram), or from within the brain (atypical or pathologic). We include real examples of clinical problem-solving processes. In particular, it is important to realize that an artificiually high qEEG index is relatively common and may result in dangerous anesthetic drug overdose. The anesthesiologist must be certain that the qEEG number is consistent with the apparent state of the patient, the doses of various anesthetic drugs, and the degree of surgical stimulation, and that the qEEG number is consistent with the appearance of the raw EEG signal. Any discrepancy must be a stimulus for the immediate critical examination of the patient’s state using all the available information rather than reactive therapy to “treat” a number.

The aim of this article is to provide an educational tool for practicing anesthesiologists to enable them to recognize the common electroencephalogram (EEG) patterns that occur during general anesthesia. The EEG has enjoyed somewhat of a renaissance since the early 1990s. This has largely been due to the development of various quantitative electroencephalogram (qEEG) monitors that use modern computer technology and complex statistical modeling techniques to generate a “number,” a qEEG index (qEEGI). This provides a simple, noninvasive way of monitoring the function of the primary target of anesthetic drugs. The Bispectral Index (BIS) and spectral entropy (M-entropy) are two commonly used examples of qEEGs. Epidemiologic studies suggest a possible reduction in the incidence of awareness and improved recovery from general anesthesia when using these monitors. In most situations, titrating anesthesia to achieve the recommended number is a reasonable clinical goal. However, as with any monitor, the processed numerical output may be misleading, especially if it is not interpreted within the clinical context. It is increasingly apparent that the complexity of neuropharmacology and neurophysiology will occasionally derail qEEGs derived from processed EEG monitors. This is recognized by the manufacturers. The Aspect Medical Systems web site notes, “It is important to emphasize that reliance on BIS monitoring alone for intraoperative anesthetic management is not recommended. Clinical judgment is crucial when interpreting BIS data. The BIS value is an additional piece of information to be incorporated with other information available for patient assessment.” Knowledge of the patient’s physiology and underlying pathology, as well as the drugs administered and surgical situation all contribute to the context within which the qEEG should be interpreted. Importantly, many of the factors that can mislead the qEEGI can be readily identified by scrutiny of the raw EEG.

We recently analyzed the effectiveness of a simple educational presentation on the ability of anesthesiologists or trainees to interpret the raw EEG. After a
15-min tutorial, the anesthesiologists in our department were able to correctly discern the difference among awake, sedated, and anesthetized EEGs with accuracy similar to the BIS and M-entropy monitors.9 In our study, the anesthesiologists made occasional mistakes, for instance, mistaking blinks for δ waves and as a consequence interpreting an awake EEG as an anesthetized EEG. However, the message we acquired from this study was that anesthesiologists are surprisingly good at interpreting the EEG even after a very brief tutorial.

The potential for both human and machine error has provided the motivation to write this article describing how the EEG patterns change with anesthesia. As this article is aimed at the practicing anesthesiologist, we have avoided neuroscience jargon as much as possible and deliberately used colloquial descriptive language. Detailed description and comparison of commercially available monitors have been covered in other publications and will not be covered in this article.9 This article is not intended to undermine the place of qEEG monitors. However, to make sense of an unexpected qEEG number, a clear mental picture of the expected EEG patterns, as well as a knowledge of the common EEG artifacts, is necessary. The anesthesiologist who wants to use the EEG as a monitor must be able to critically scrutinize the raw EEG.

GENESIS AND ANALYSIS OF THE EEG

A formal EEG performed for diagnostic neurological purposes uses a montage of multiple electrodes over the whole scalp. This would be impractical during anesthetic delivery. Fortunately, anesthetic drug administration causes an increase in frontal cortical EEG activity (frontal predominance), so that the forehead is both an easy and a worthwhile site to measure the EEG effects of anesthetic drugs.9 The EEG electrode montage used in our setting is a simple series of three or four electrodes placed on the forehead and temple: positive, negative, and reference. Some devices have more than three electrodes to better define electromyographic (EMG) activity and spatial changes in the EEG across the cortex.

Excitatory pyramidal neurons are mainly arranged side-by-side, in the fifth layer of the cerebral cortex, with their dendritic trees extending upward and then parallel to the surface of the cortex.10 The synaptic activity in the dendrites causes partial depolarization or hyperpolarization, creating rapidly changing potential differences between one point on the scalp and another. These voltage fluctuations are the predominant basis of the EEG signal rather than axonal action potentials. The activity in the dendritic trees of approximately 50–500,000 pyramidal neurons are reflected in each EEG electrode. The scalp electrodes also detect potential differences caused by other (often larger) current sources. These include muscle activity (frontalis, extraocular eye muscles, and heart) and induced potential differences due to external current sources, such as room wiring, and electrical devices, such as diathermy. These are important sources of artifact in the EEG and will be covered in more detail later. The EEG is a microvolt-range signal; in contrast, much of the artifact will be of a millivolt magnitude. This makes the quality and consistency of the electrode to skin connection essential to the reliable interpretation of the signal.

The EEG has no fixed repeating pattern, changing randomly over time. However, with steady levels of anesthesia or wakefulness, it will have some constant statistical features over time. For instance, the average amplitude of the waveform when awake will be low. This is an example of analysis in the time domain. Another time domain example is the burst suppression ratio: the ratio of the amount of time the EEG is suppressed against the amount of time it is bursting. Analysis in the frequency domain is a universal component of qEEG analysis. A segment of EEG is mathematically deconstructed into sine waves of varying frequency, amplitude, and phase. The original EEG segment can be reconstructed by adding these sine waves together. Traditionally recognized EEG frequency bands are outlined in Table 1.11 Information about the relative contribution of each frequency band to the EEG segment being analyzed is often presented as a power spectrum with frequency on the x axis and power estimated by amplitude squared on the y axis. The high frequency α and β waves predominate during wakefulness, whereas the slower δ and θ waves predominate during sleep or anesthesia (Table 2). QEEGs analyze the signal in both time and frequency EEG domains.9,12

Table 1. Electroencephalogram Wave Categorization by Frequency

<table>
<thead>
<tr>
<th>Wave category</th>
<th>Descriptive term</th>
<th>Frequency (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>δ</td>
<td>Slow</td>
<td>0.5–3.5</td>
</tr>
<tr>
<td>θ</td>
<td>Slow/medium</td>
<td>3.5–7.0</td>
</tr>
<tr>
<td>α/spindles</td>
<td>Medium</td>
<td>7.0–13.0</td>
</tr>
<tr>
<td>β</td>
<td>Fast</td>
<td>13.0–30.0</td>
</tr>
<tr>
<td>γ/β</td>
<td>Fast</td>
<td>30.0–80.0</td>
</tr>
</tbody>
</table>

Table 2. Summary of Expected Electroencephalogram Patterns from Awake to Deeply Anesthetized

<table>
<thead>
<tr>
<th>State</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awake</td>
<td>Small amplitude, high frequency “fuzzy” look</td>
</tr>
<tr>
<td></td>
<td>Blinks and eye movements</td>
</tr>
<tr>
<td></td>
<td>Sometimes high amplitude, high frequency EMG</td>
</tr>
<tr>
<td></td>
<td>Alpha oscillation if relaxed and eyes closed</td>
</tr>
<tr>
<td>Drowsy</td>
<td>Loss of EMG, eye movements and blinks</td>
</tr>
<tr>
<td></td>
<td>Increasing amplitude and discernable medium waves</td>
</tr>
<tr>
<td>Light anesthesia</td>
<td>Bigger slower waves that wax and wane over tens of seconds</td>
</tr>
<tr>
<td></td>
<td>Spindles</td>
</tr>
<tr>
<td>Deep anesthesia</td>
<td>Longer lasting, slower spindles</td>
</tr>
<tr>
<td></td>
<td>Burst suppression</td>
</tr>
<tr>
<td></td>
<td>Isoelectricity</td>
</tr>
</tbody>
</table>

EMG = electromyography.
Recognizing the EEG patterns in themselves is not enough. These are simply pointers to the things that we are really interested in, which are the underlying anesthetic-induced disturbances in neurobiological function. There have been many studies that document, in some detail, the progression of EEG changes that occur with natural sleep. The changes that occur under anesthesia are similar but not identical. To grasp the nature of these changes, an appreciation of the underlying neurophysiologic background is essential. For each of the stages described later, a brief description of the neurophysiologic basis of the EEG pattern is included in the boxed section (Boxes 1–3). There is significant variation in EEG pattern among drugs, electrode positions, and individuals. The patterns we describe are derived from sleep research, anesthetic research, and our experience with EEG monitoring during general anesthesia. As with any waveform, the appearance of the EEG can be markedly changed by manipulating the sweep speed and the vertical scaling. We have tried to standardize the figures in this article to be similar to those seen on routine EEG monitors.

**Awake**

The EEG of an awake subject consists of high frequency, low amplitude waves (Fig. 1 and Box 1). These look like a fuzzy flat line. However, EMG interference from facial and ocular muscles is common and results in both a wandering baseline and extraneous high amplitude, high frequency activity. Blinks are represented by a sharp deflection and then an exponential return to the baseline. Eye movements usually create a large deflection to both sides of the baseline before returning. Smiling or grimacing generates increased high frequency activity from facial and temporalis EMG. Multiple examples of the range of awake EEG patterns one might expect to encounter can be found in Appendix Figure 1 (see Supplemental Digital Content 1, which shows an example of electroencephalogram recordings obtained during the awake state showing predominantly artifact, http://links.lww.com/A1183).

**EEG PATTERNS**

The EEG looks “fuzzy” because the individual fast waves are of low amplitude and blurred together (when displayed at sweep speeds of 25 mm/s). The classic rhythm of relaxed wakefulness is predominately occipital and not commonly seen using frontal electrodes in anxious preoperative patients.

**Sedated—Becoming Anesthetized**

As the sedative/hypnotic drug concentration increases, there is a consistent sequence of EEG changes. Initially, there is an increase in β amplitude in the frontal EEG. With deeper sedation, the β activity slows to spindle-like/α waves and then slows further to the θ range, with the loss of α and β waves (Fig. 3 and Box 2). This induction sequence is displayed in Figures 2 to 4. Further examples of EEG recordings exhibiting strong spindle-like activity can be found in Appendix Figure 2 (see Supplemental Digital Content 2, which shows an example of electroencephalogram recordings showing strong spindle-like activity, http://links.lww.com/A1184).
Box 2. Neurophysiology of sedation – spindle-like activity

The principle anesthetics (propofol, volatiles) have pronounced activity at gamma-aminobutyric acid (GABA) receptors. These drugs increase the inhibitory action of GABA, resulting in suppression of action potential generation and hyperpolarization of cortical and thalamic cells. This pattern is similar to slow wave sleep.22,23 Neurons in the cerebral cortex and the thalamus are inextricably linked through cortico-thalamo-cortical connections. As a result, changes in the pattern of activity within the thalamus are reflected in the cortex and detectable by the EEG. As the neurons in the cortico-thalamo-cortical circuits become hyperpolarized, the thalamic neurons move from a continuous firing mode to a burst firing mode. The EEG manifestation of this is the appearance of short bursts of activity with a frequency of around 7–14 Hz which wax and wane over time (Figures 3 and 4). In the context of sleep, these waves are called “sleep spindles,” and they are the hallmark of natural sleep onset.13 Similar “spindle-like” activity is seen with anesthesia. Spindles can start in the thalamus and spread to the cortex or vice versa. They appear to be a global EEG event, meaning they are readily detectable by the frontal EEG. Spindles tend to be synchronous across the cortex and in the setting of general anesthesia the appearance of spindle-like activity should coincide with patients becoming unconscious due to anesthetic drugs.17–22,24

Figure 3. Slow waves are beginning to predominate although there are still faster waves visible. At the 5-s mark, there is a short burst of spiky waves that probably represent a sleep spindle. Blinks and eye movements are absent and there is little electromyography. This patient will likely appear asleep. Should painful stimulation occur, this electroencephalogram could change to appear more awake: cortical arousal in response to the stimuli. Movement would also occur although explicit recall of the pain would be unlikely.

Figure 4. Electroencephalogram during adequate general anesthesia. Sleep spindles are present throughout the trace with a consistent, repetitive slow wave background.

Other EEG signs consistent with induction of anesthesia include absence of blinks and eye movements, disappearance of EMG, and overall slowing in the frequency of the EEG. These changes are all easily discernable. The baseline will remain relatively flat as the patient first becomes unconscious. With increasing depth of anesthesia, slow δ waves (1–4 Hz) make the whole EEG slowly wander up then down around the baseline.

Anesthesia

A primary difference between general anesthesia and natural sleep is lack of movement in response to painful stimulus. The EEG is a relatively poor predictor of responsiveness to nociceptive stimulation. Movement, in the presence of a low qEEGI, reflects the fact that immobility during anesthesia is related primarily to anesthetic effects on the spinal cord rather than the cortex. The EEG does not monitor spinal cord anesthetic effects. If a patient is medicated enough to cause sedation (sleeping), their qEEGI may be low. If a noxious stimulus is given to this patient, he or she will wake up and the EEG will change completely. In contrast a lack of movement, despite a relatively high qEEGI in an unparalyzed patient, may reflect that the EEG is not very sensitive to the effects of opioids or nitrous oxide. These potent analgesics reduce afferent input to the brain and hence reduce the occurrence of movement at a given anesthetic depth. When isoflu- rane was used as the sole anesthetic (targeting a BIS of 40), 50% of the patients moved in response to a noxious stimulus. Conversely, if BIS values were kept at 40 using a combination of opioid plus isoflurane, propofol, or nitrous oxide, <10% of patients moved.25

Box 3. Neurophysiology of the anesthesia – delta waves

Delta waves are the hallmark of slow wave sleep and deeper anesthesia. They represent slow, travelling waves of synchronous hyperpolarization (alternating with depolarization), initiated mainly in the prefrontal cortex.26 Burst suppression (Figure 6) and isoelectricity are features of progressively deeper anesthesia. Neither occurs during natural sleep.

The presence of spindle-like waves and background slow (δ) waves, with no fast waves, are probably the most important EEG signs of anesthesia.
(Fig. 4 and Box 3). Spindles become slower and longer as anesthesia deepens and the background shape of the EEG approximates a sine wave of 1–6 Hz.27 Further examples of EEG recordings exhibiting strong δ wave activity can be found in Appendix Figure 3 (see Supplemental Digital Content 3, which shows an example of electroencephalogram recordings showing a predominance of δ activity, http://links.lww.com/A1185).

Figure 5. Response to surgery. This patient was anesthetized with isoflurane and fentanyl and shows a conventional arousal electroencephalogram (EEG) pattern in response to surgical incision, which caused the spindles and slow waves to become smaller and an increase in the fast waves. Recall would be unlikely. However, assuming that the patient is otherwise stable, this change in EEG pattern suggests anesthesia should be deepened slightly. Note sometimes, there is an opposite effect: an increase in δ wave activity in response to noxious stimuli (Fig. 11). RE = response entropy.

Figure 6. The first 6 s of this electroencephalogram is an isoelectric flat line followed by a burst of spindle-like activity. These are the characteristics of burst suppression and represent electroencephalogram (EEG) signs of very deep anesthesia.

Administration of higher doses of anesthetic causes a phenomenon known as burst suppression (Fig. 6). This is a period of spindle-like or fast spiky activity (burst) followed by a period of flat line (suppression). Burst suppression represents deep anesthesia and is not commonly targeted therapeutically, except to obtain metabolic cerebral suppression for cerebral protection or the suppression of seizures. Even higher doses will induce isoelectricity (a continuous “flat” line). It represents a complete absence of neuronal communication due to either suppression by anesthetics or a severe physiologic aberration (neuronal metabolic failure). Dosing to achieve burst suppression will usually result in patients who are not only unconscious but also do not move in response to noxious stimuli. Commonly, it will also result in hypotension, slow recovery times, and excessive consumption of general anesthetic drugs.

ARTIFACTS AND PROBLEM SOLVING DURING ANESTHESIA

The practical skills required for the correct interpretation of the EEG signal during anesthesia are the same as those required for the use of any physiologic monitor. As reflected in the title of this article, the skills have an algorithmic component (the “science”), but also require some judgment (the “art”). The anesthesiologist should establish the monitor and examine the raw EEG before induction, then look to see how both the raw EEG and the qEEGI change in response to induction of anesthesia and to subsequent noxious stimulation. Noxious stimulation may result in no change, increase, or decrease in qEEGI (see paradoxical cortical arousal below and Figures 5 and 11).28 When the level of surgical stimulation changes, the raw EEG can change abruptly but the change in qEEGI number is delayed by 14 and 155 s.29 The following paragraphs summarize the thought processes that are required for the safe use of an EEG monitor.

1. When using a qEEG monitor, the anesthesiologist must repeatedly confirm that:
   a. The qEEGI number is consistent with the apparent state of the patient, the doses of various anesthetic drugs, and the degree of surgical stimulation.
   b. The qEEGI number is consistent with the appearance of the raw EEG signal.

2. If there is a discrepancy, then the following secondary questions must be answered:
   a. Is the EEG monitoring system intact?
   b. Is there interference from outside the head?
   c. Is there interference from the head but outside the brain (i.e., frontal EMG)?
   d. Is there interference from within the brain (i.e., the EEG is atypical or pathologic)?

The EEG Monitoring System

One must always check the basics: that the electrode-skin impedance is acceptable (that the skin
has been adequately dewaxed) and that the electrodes are not being shorted out by fluids. Most EEG monitors have automatic electrode impedance checking built into their systems.

**Artifacts from Outside the Head**

These artifacts most commonly include (i) “noise” from electrical equipment, (ii) external pacemakers, (iii) electrocardiogram (ECG) (Fig. 7), (iv) diathermy (Fig. 8), and (v) surgical movement of the patient, hammering, or drilling. These are described in detail by Dahaba.6 Power-line artifact is probably the largest source of potential exogenous electrical artifact. The patient’s body acts like an aerial and the wiring in the walls of the operating room may induce currents. This causes a potential difference that will be measured by the EEG electrodes. Fortunately, as long as each electrode has good contact and similar impedance, then the power-line artifact affects all electrodes equally and the artifact will be reduced or eliminated. It is usually possible to stop the artifact by briefly halting surgery or turning off some ancillary device. If the depth of anesthesia is adequate, the EEG signs of anesthesia will become apparent immediately and the qEEGI number should decrease during the subsequent 1–2 min. It may be advisable to repeat this process of inspecting the “clean EEG” periodically. The Aspect (BIS) monitors use complex artifact recognition processes, including templates for blinks and the R wave of the ECG.11 EEG signal, which is thought to have lots of interference (e.g., diathermy), is usually excluded from analysis by qEEGI. The amount of acceptable EEG signal is displayed in the BIS monitor as the signal quality index.

High frequency interference occurring on an isoelectric EEG may fool the qEEGI artifact rejection algorithms. If such a segment of “false” EEG is not rejected, the qEEGI number will be high, potentially indicating the “awake state.” If this situation is not recognized by the anesthesiologist, he or she will be encouraged to deepen what is already deep anesthesia with potentially catastrophic consequences. Any discrepancy between what the anesthesiologist expects and the number that the qEEGI monitor displays must be a stimulus for the immediate critical examination of the patient’s state using all the available information rather than reactive therapy to “treat” a number.

**Artifacts from the Head Outside the Brain: EMG**

Frontalis, masseter, or extraocular eye muscle EMG is by far the most common artifact to affect qEEGI (Fig. 9). Whether EMG is truly an artifact or a source of useful additional information is debatable. In some circumstances, detection of frontalis “grimacing” may be considered a useful indication that the analgesic component of general anesthesia is inadequate. This approach has been promoted in some commercial monitors but has not been widely validated. Typically, EMG occurs at the frequency range of 10–300Hz, which overlaps the same frequency spectrum as an awake EEG. It cannot be filtered out completely and...
Figure 10. Seizure activity is high frequency but also very high amplitude (note the scale is 500 microvolts unlike the previous electroencephalograms [EEG] which have all been 100 microvolts) EEG. This is an electroconvulsive therapy seizure but is clinically indistinguishable from a seizure caused by epilepsy or seizure-generating anesthetic drugs (e.g., high concentration sevoflurane). Quantitative EEG indices do not recognize seizures. They may reject the EEG as artifact or give a falsely high number as the high frequency EEG is misinterpreted as awake.

will usually increase the qEEGI number, which can be misinterpreted as indicative of an awake patient.

The appropriate responses by the anesthesiologist to elevated EMG are complex and may include changing nothing, increasing the hypnotic or analgesic dosage, or sometimes even giving muscle relaxants. The pattern recognition capabilities of the human expert can look at the raw EEG of an anesthetized patient with a lot of EMG and can usually separate out the background pattern of adequate anesthesia (spindles or slow waves) from the superimposed high frequency EMG activity (Fig. 9). If anesthetic depth is thought to be satisfactory on the basis of other clinical information, a muscle relaxant will eliminate EMG, enabling more accurate qEEGI assessment. It must be noted that the subgroups of the frontalis muscle may be relatively resistant to neuromuscular blockade. One should be very wary. Several studies have shown that the administration of muscle relaxant alone can decrease the BIS or M-entropy values. In one report, awake volunteers were given a depolarizing muscle relaxant, which caused marked reductions in qEEG (BIS, A-1000), despite no sedation or amnesia whatsoever. The reason a muscle relaxant might decrease the BIS value in an awake individual is unclear, but it is postulated to be either a reduction in the EMG amplitude (the awake EEG being misinterpreted as isoelectricity or burst suppression) or a reduction in afferent input to the brain from muscle spindles. It is important to note that in neither of the above cases did the raw EEG show any signs of anesthesia, despite confusing the qEEGI (i.e., visual examination of the raw EEG would clearly distinguish these subjects as being fully awake!). This is obviously a cause for concern because awareness is more serious in paralyzed patients. In practice, if the EMG is falsely elevating the qEEGI, it is important to check the anesthetic delivery. If the anesthesiologist is completely sure that anesthetic delivery is adequate (e.g., >0.8 minimum alveolar concentration end-tidal volatile anesthetic), then a dose of muscle relaxant could be given, the EEG reexamined and the changes in the qEEGI over the subsequent few minutes noted to ensure the response is consistent with expectations (i.e., the qEEGI should decrease to values reliably associated with general anesthesia). There are many reasons for increased muscle tone during anesthesia. It is the authors’ experience that propofol total IV anesthesia is much more prone to EMG interference than volatile-based anesthetics (which have a different spinal cord effect). Also giving high doses of opioids in this setting can increase EMG by their rigidity effects and paradoxically increase qEEG.

Artifacts Within the Brain: Atypical or Pathologic EEGs
These can be the most difficult confounders of qEEGI to resolve because there are generally no external clues as to the cause of the unexpected qEEGI. A high index of suspicion is important, as is accurate knowledge of the patient’s current physiology, pathology (including co-morbidities), surgical procedure, and drugs administered. An abnormal preanesthetic EEG or qEEGI will help identification of this problem. The following are common artifacts from within the brain, which can mislead qEEGI but not necessarily an educated anesthesiologist who pays attention to the EEG.

Low Amplitude EEG
A low amplitude EEG can either be genetically predetermined, drug-induced, or pathologic. An estimated 5%–10% of the population has a genetically determined low amplitude EEG that can be misinterpreted by qEEGIS. One case report demonstrates a fully awake and conscious volunteer with a BIS value of 40. Drug-induced low amplitude EEG has been observed during the washout phase of both remifentanil and volatile anesthetics, and the low amplitude (awakening) EEG was misinterpreted as burst suppression resulting in a paradoxical decrease in qEEGI.

Seizure Activity and Postictal State
Seizure activity (Fig. 10) can occur as a result of abnormal physiology, cerebral pathology, electroconvulsive therapy, or drugs. A significant clinical concern arises when anesthetic-induced seizures are misinterpreted by qEEGIS. Sevoflurane, a widely used volatile anesthetic, is one such example. During deep levels of sevoflurane anesthesia, qEEG indices may be elevated due to the high frequencies that are often present in the large amplitude seizure activity. After electroconvulsive therapy, patients in a postictal state can have very low qEEGI despite being conscious with eyes open. The cause is an EEG pattern consisting predominantly of slow waves similar to those found during deep anesthesia.

Variable δ Activity
Sometimes there is variation in δ activity during stable anesthesia unrelated to surgical stimulation. The cause remains unknown. Generally, qEEGIS will...
fail for a period of time until the EEG returns to its previous appearance. These are rarely of clinical significance. However, beware if slow waves or isoelectricity persist during minimal anesthetic delivery, this may represent significant cerebral pathology or physiologic derangement.

Paradoxical δ Activity
A surprising EEG phenomena known as paradoxical cortical arousal (Fig. 11) may mislead qEEGs. In about one third of patients under general anesthesia, noxious stimulation causes an increase in large, slow δ waves rather than the faster waves usually associated with increased wakefulness. This commonly causes qEEGs to decrease when all other contextual factors indicate that the qEEGI should increase.

Cerebral Pathology
Because the qEEGs have been formulated using healthy patients, they can behave unexpectedly in the presence of neurological disease. There are numerous studies reporting significant EEG abnormalities in psychiatric patients. Patients with Alzheimer’s and vascular dementia, and patients with organic delusional states, have increased slow waves and decreased fast waves in their awake EEG. Schizophrenics also commonly have an increase in frontal slow waves with a decrease in α waves. Medication can confound the EEG changes in schizophrenia, with neuroleptic drugs being shown to increase either slow or fast EEG activity in different studies. Alcohol and drug use can cause a myriad of EEG changes. Alcoholism will generally increase β waves, whereas cocaine and cannabis increase α waves. Cerebrovascular disease can alter EEG patterns because EEG slowing is highly correlated with decreased regional cerebral blood flow or metabolism. The EEG may even be sensitive enough to detect mild degrees of ischemia that cause dysfunction without infraction.

ADJUNCTIVE ANESTHETIC DRUGS: EFFECTS ON THE EEG
To be effective in interpreting changes in the raw EEG, the anesthesiologist must know what changes can be expected in response to anesthetic and anesthetic-adjuvant drugs.

Ketamine
The N-methyl-D-aspartate receptor antagonist ketamine adds hypnotic and analgesic anesthetic components that are not accurately reflected in the qEEGI. If ketamine is administered in the presence of background GABAergic anesthesia, it causes an increased amount of high frequency EEG activity (Fig. 12). This is visible on the raw EEG and consistently causes an increase in both BIS and M-entropy values. The clinical implication is that qEEGI will increase, falsely suggesting that the patient has become more lightly anesthetized, whereas the opposite has actually occurred. This can result in unnecessary anesthetic overdose unless the cause of the EEG change is recognized.

Nitrous Oxide
Nitrous oxide appears to have minimal effect on the EEG. A majority of studies show that unconsciousness induced by a predominantly nitrous oxide effect
occurs at high BIS or M-entropy values.\textsuperscript{54} Similarly, the addition of nitrous oxide to a stable level of GABAergic anesthetic has minimal effect on the EEG.\textsuperscript{55} Some studies have even suggested slight EEG activation with an increase in BIS values.\textsuperscript{56} This is contrary to the clinical effect observed, because nitrous is well proven to be minimum alveolar concentration additive to other anesthetics.\textsuperscript{57} Somewhat confusingly, nitrous oxide has also been associated with paroxysmal decreases in BIS values 5–10 min after discontinuation,\textsuperscript{56} the opposite of the clinical effect again. The raw EEG in these situations shows an increase in slow $\delta$ and $\theta$ waves suggestive of deepening anesthesia. The clinical implication is that qEEG monitoring will not recognize the effect of nitrous oxide at clinically used concentrations.

**Opioids**

Opioids have a variable effect on the EEG because they predominantly affect noncortical structures. Small doses produce minimal EEG changes. Larger doses can produce EEG slowing.\textsuperscript{58} Although opioids alone are poor at preventing intraoperative recall, their addition to GABAergic anesthetics significantly reduces the dose of anesthetic required to prevent both recall and responsiveness.\textsuperscript{39} Studies show that adding opioids to an anesthetic will either decrease the BIS or M-entropy number, or reduce the likelihood of movement or awakening at a given number.\textsuperscript{59,60} It has been suggested that a BIS value of $>60$ may be acceptable when a high-dose opioid, low-dose GABAergic drug anesthetic technique is used.\textsuperscript{61} Conversely, if no opioid is used, a BIS of 40 may be insufficient to prevent movement, although recall is extremely unlikely.\textsuperscript{62}

**Other Drugs**

Other drugs commonly used during anesthesia can interfere with qEEGs. Epinephrine and ephedrine, but not phenylephrine, have been shown to increase BIS values when administered during sedation or anesthesia.\textsuperscript{63,64} It is the authors’ experience that intensive care unit patients taking high doses of inotropes (most commonly norepinephrine or epinephrine) often have high qEEGs despite apparently adequate anesthesia. As these endogenous neurotransmitters are important in corticothalamic interactions, this is perhaps not surprising. Whether the altered cortical activity results in an increased risk of awareness remains unknown. Alpha-2-agonists, such as clonidine and dexmedetomidine, seem to have similar EEG effects as the GABAergic drugs, despite quite a different mechanism of action. Loss of $\alpha$ rhythm with a slow $\delta$ wave predominance occurs with a corresponding decrease in qEEG.\textsuperscript{65,66} Etomidate, a GABAergic IV induction drug, used predominantly in hemodynamically compromised patients also displays the typical EEG patterns associated with general anesthesia.\textsuperscript{67}

**What to Do with an Unexpectedly High QEEGI Number?**

We use the following clinical scenario as a practical example of some of the thought processes (algorithmic and nonalgorithmic) that the anesthesiologist might go through when faced with a patient with an unexpectedly high qEEGI. We use this example because a high qEEGI is much more common than an unexpectedly low qEEGI. During induction of propofol or sevoflurane anesthesia, between 40% and 90% of all patients will become unresponsive at a BIS value of $>70$.\textsuperscript{68–71} During non–BIS-driven maintenance of anesthesia, the BIS is $>70$ between 12% and 50% of the time.\textsuperscript{3,25,72}

A healthy 73-year-old female patient presented for reduction and fixation of a tibial plateau fracture. General anesthesia was induced with fentanyl (250 $\mu$g IV) and propofol (70 mg IV). Rocuronium (40 mg IV) was used to enable tracheal intubation and positive pressure ventilation of the lungs. Anesthesia was maintained using sevoflurane in an air–oxygen mix. Monitoring consisted of noninvasive arterial blood pressure (BP), ECG, expired gas analysis, and frontal EEG (M-entropy). The preinduction EEG looked normal. Figure 13 (upper) shows the EEG trace from the patient 15-min postinduction and 3 min before surgery. At this stage, the patient had a BP of 90/40 mm Hg and a heart rate (HR) of 52/min. The end-tidal sevoflurane concentration was 1.55%, and the patient would be likely to have more than adequate brain concentrations of fentanyl. However, we can see that the response entropy (RE) was appreciably increased ($\sim$80) above that which would normally be recommended ($\sim$20–50). As regard “depth of anesthesia” in this patient, the conundrum for the clinician was to resolve whether:

1. The qEEG number is consistent with the apparent state of the patient, the doses of various anesthetic drugs, and the degree of surgical stimulation?
2. The qEEG number is consistent with the appearance of the raw EEG signal?
The answer to the first question is, “No, the patient has received quite a generous dose of various anesthetic drugs (confirmed by the hypotension) and is not surgically stimulated at present. We would have expected a RE value to be <60 at this point in time.”

The answer to the second question is, “Yes, although there are some slow waves in the raw EEG signal, there is clearly quite a lot of high frequency (“fuzziness”) activity.” What is the cause of these fast waves? A careful check by the anesthesiologist found that the qEEG monitoring system was intact and that there were no extracranial sources of interference. EMG should have been largely abolished by the dose of rocuronium. In this case, it can be assumed that the high frequencies in the EEG signal were truly originating in the brain. A power spectrum of the EEG (data not shown) demonstrated a band of activity within the β range (20–25 Hz). The patient had not been given any nitrous oxide or ketamine that could clearly explain the high frequencies, and there was no obvious epileptiform activity.

There was no obvious problem with anesthetic drug delivery. The end-tidal sevoflurane concentration and the patient’s clinical signs suggest adequate hypnosis in this (unstimulated) state. There are two further questions that must be asked:

1. Should the clinician ignore these findings and increase the sevoflurane delivery on the basis of the elevated RE value?
2. How will this change when the surgeon starts the operation?

Because of the presence of the background slow activity seen in the raw EEG and the fact that the anesthesiologist was sure that there had been adequate delivery of anesthetic drugs, it would be reasonable to ignore the RE value and continue with the anesthetic unchanged. However, the raw EEG did not show signs of deep anesthesia (spindles or large δ waves), and therefore it was felt that it was possible that the patient might show a deleterious autonomic response to the impending incision. The attending anesthesiologist therefore elected to give some vasopressor (IV metaraminol 0.5 mg) to treat the hypotension, and in anticipation of the surgical stimulus, increased the sevoflurane delivery slightly. After the incision, the BP increased (BP = 140/70) and the HR remained stable (HR = 53), and the RE decreased⁵⁷ (Fig. 13, lower). The lack of HR response to the incision and the appearance of good amplitude spindle-like patterns indicated adequate suppression of nociceptive stimulation of the cardiovascular system and cortical arousal. Surgery progressed uneventfully and the patient had no recall of intraoperative events. Other resources for problem solving an unexpected qEEGI can be found on the Aspect web site (www.biseducation.com) and in a recent article by Voss and Sleigh.⁷³

FINAL COMMENTS

QEEG monitors provide a practical and direct measure of the functional state of the cerebral cortex during general anesthesia. Unfortunately, it is not possible to safely monitor a patient by blind obedience to the processed number. If an anesthesiologist has little understanding of (i) the expected raw EEG changes during anesthesia, (ii) the sources of non-EEG artifact, and (iii) the unusual EEG patterns which may occur, then the use of these monitors may well result in more harm than good. Knowledge and common sense are integral to the effective use of any patient monitor. The thrust of this article has been to educate clinicians, so that they are better equipped to problem solve when faced with an unexpectedly high or low qEEGI number. With experience, a “sleepy EEG” waveform despite an ongoing surgical stimulus becomes just as reassuring as the capnograph and plethysmography waveforms.

REFERENCES

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