EDITORIAL

What does the bispectral EEG index monitor?

Depth of anaesthesia is an old concept originally based on the depressant effects of volatile anaesthetics on the central nervous system. As the dose of anaesthetic is increased, there is progressive loss of consciousness and suppression of somatic and autonomic responses to noxious stimuli. It seemed logical to search for a measure of central nervous system depression that would serve as a monitor of anaesthesia. The electroencephalogram (EEG) was much studied and a number of signal processing techniques were developed to facilitate interpretation [1]. Unfortunately, none of the early processed EEG derivatives (95% spectral edge frequency or median power frequency) were able to correlate reliably with consciousness, movement or autonomic responses. In the *European Journal of Anaesthesiology*, Driessen *et al.* concluded that the bispectral Index (BIS), the latest EEG derivative, also did not predict the haemodynamic response associated with endotracheal intubation and stenotomy [2].

To understand Driessen *et al.*'s findings, one must review the evolution of BIS. Unlike early processed EEG variables, BIS is derived from the bifrontal EEG recordings collected from a huge group of subjects ($n > 5000$) sedated with different anaesthetics [1,3]. These EEG waveforms were then analysed off-line according to three features:

(a) *Burst suppression ratio.* This is a time-domain feature that quantifies the extent of electrical silence during deep anaesthesia.

(b) *Relative alpha/beta ratio.* This is a frequency-domain feature and contributions from these frequency bands (alpha 8–13 Hz, beta 13–30 Hz) are often seen during light sedation.

(c) *Bicoherence* of the EEG. This describes the phase coupling relations between individual waves. In simple terms, a signal with strong phase relations and a high bicoherence value implies a common generator and may be associated with moderate sedation.

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Using a multivariate regression model, scientists from Aspect Medical Systems (Natick, MA, USA) have transformed the relative contributions of each feature into a linear numeric index (BIS), ranging from 0 (isoelectric EEG) to 100 (fully awake).

Therefore, BIS is a statistical function that has been tuned, with successive software revisions, to correlate with the degree of sedation produced by isoflurane [4], sevoflurane [5], propofol [4,6–8], and midazolam [4,9], even in the presence of opioids [4,7]. The BIS that prevents 50% of subjects from responding to verbal command ranges from 67 to 79 [4–9]. Statistically, it would be extremely unlikely for a patient to be aware when BIS is less than 50 (and, in fact, there has not been a single case of frank awareness at this level). On the contrary, recovery of consciousness is expected as BIS rises above 90. The BIS that prevents implicit memory is between 84–91 [4,6].

BIS therefore differs from other EEG derivatives, in that it is designed to be a measure of sedation and not of anaesthesia as a whole. It appears robust enough to monitor sedation produced by common anaesthetics in combinations, although ketamine and nitrous oxide *per se* are currently the exceptions [10–12].

Nevertheless, early in the development of BIS, researchers did in fact try to correlate the index with movement. Although BIS may still predict somatic and autonomic response to noxious stimuli better than other EEG measures, the performance is significantly worse compared with its correlation to sedation [4,13–15]. This endpoint was abandoned by Aspect Medical Systems in 1993, but it has obviously influenced and perhaps confused the literature on this subject.

The lack of correlation between EEG derivatives and somatic and autonomic response is not surprising given the results of studies that evaluated the spinal cord as a site of anaesthetic action. In these experiments, the dose of anaesthetics required to

abolish purposeful response to noxious stimuli in decerebrate rats was identical to that in intact animals [16, 17]. Although these data cannot be directly extrapolated to humans, it appears that unresponsiveness to peripheral noxious stimuli is independent of cortical structures. Logically, it would be unrewarding to monitor the cortical EEG when the primary endpoint is determined at a subcortical level. Nevertheless, EEG arousal following a painful stimulus can often be quantified by an absolute increase in BIS and this has been a useful measure of intraoperative analgesia [7, 18]. Theoretically, if one was interested in the prediction of autonomic responses to noxious stimuli, it may be possible to start afresh and extract signals from the EEG that correlate best with this endpoint and derive a *brand new index.*

So, what does BIS really monitor and how should it be applied? BIS, as an average over the last 30 s, is an indicator of a very recent degree of sedation. Contrary to common beliefs, it should not be regarded as a predictive index of future events. When presented with a BIS number, the anaesthetic regimen and clinical circumstances must also be considered. An unstimulated patient equilibrated with isoflurane 0.5% or propofol 1 μg mL^{-1} is likely to be asleep and will have a low BIS value. Under these circumstances, a sudden skin incision is expected to cause movement, exaggerated autonomic responses and possible awakening (with a subsequent rise in BIS). However, such responses are in no way indicative of BIS failure. We also know that a patient equilibrated with isoflurane 4% or propofol 12 μg mL^{-1} is likely to be unconscious. In this situation, a high BIS value should lead one to look for an artefact. Thus, BIS is most useful when one is using a general anaesthetic agent at concentrations just sufficient to provide unconsciousness. This is particularly important with intravenous agents where drug concentrations cannot be measured concurrently.

There is another situation that BIS monitoring would become important. In scenarios in which inter-individual pharmacokinetic and pharmacodynamic variability of anaesthetics are known to be large (e.g. during cardiopulmonary bypass), one would expect that standardized dosing regimens should produce different effects in different patients. If one believes in the BIS as an endpoint of the sedative effect, then it is possible to titrate individually the dose of general anaesthetic to provide unconsciousness. The suppression of somatic and autonomic responses will require separate titration of the muscle relaxant and analgesic. Taken together, BIS-guided anaesthesia (in over 600 patients) has been associated with lower consumption of anaesthetics, earlier awakening and faster recovery [19–23] and many other potential applications are being explored [24–26].

There are limitations with BIS monitoring, as with all new technologies, during clinical anaesthesia. A number of environmental and physiological factors may affect BIS performance. Electrical 50-Hz mains interference, and electrocardiographic and electromyographic artefacts introduce high-frequency signals and are the major source of errors [27]. EEG slowing with hypothermia and cerebral ischaemia can appear identical to that of deep sedation and will decrease BIS. Unless these factors are carefully corrected, serious misinterpretation can result.

Will BIS monitoring prevent awareness? This will be difficult to prove. Given that BIS indicates a probability of unconsciousness, awareness may depend on how closely the anaesthetist chooses to titrate the anaesthetic to test the limits of probability.

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