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"I would have everie man write what he knowes and no more."—Montaigne

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Editorial I

Is there any alternative to the Bispectral Index Monitor?

The importance of having a reliable indicator of depth of anaesthesia has long been realized by anaesthetists.[1] Initially, the haemodynamic response to laryngoscopy, tracheal intubation and/or skin incision was used to assess the anaesthetic depth. Subsequently, electroencephalography (EEG) and the various forms of processed EEG (e.g. spectral edge frequency and total power) were used, none of which was very successful. In 1997, Aspect Medical Systems (Natick, MA, USA) introduced a device that displays a single 'bispectral index' or a BIS value, which measures the depth of anaesthesia. Over the years, the usefulness of the BIS monitor in having a high probability of correctly predicting the absence of consciousness during general anaesthesia has been recognized.[2–4] Although there is no evidence that monitoring the depth of unconsciousness prevents awareness, it is conceivable that, by maintaining a sufficient depth of unconsciousness, this will be achieved. Indeed, the BIS monitor has established itself mainly as a means of minimizing the incidence of awareness. In addition, the BIS has been helpful in providing more rapid awakening from general anaesthesia in ambulatory and cardiac surgery.

While most anaesthetists are interested in having an easily interpretable depth of anaesthesia monitor, one wonders how many are actually interested in knowing how the magic number displayed by the BIS monitor is derived. Very few anaesthetists understand the science and engineering of recording and processing the EEG. The curiosity of some anaesthetists is limited to knowing that the BIS is some form of mathematical analysis of the EEG (processed EEG), while others know that it uses a higher order of statistical analysis (the bispectrum). Nevertheless, concern about how exactly the BIS number is derived continued and a useful review by Rampil[5] describing how it does work alleviated some of these concerns. This issue of the *British Journal of Anaesthesia* contains an article by Miller and colleagues,[6] which is testimony to the fact that some anaesthetists have a keen interest in understanding the methodology used in the development of the BIS monitor and the alternatives to it.

Let us briefly consider (on the basis of information that is currently available) how the BIS is derived. Unlike earlier methods, which relied on tracking and processing a single parameter of the EEG, the BIS calculates three subparameters: burst suppression [with two separate algorithms, viz. the burst suppression ratio (BSR) and QUAZI]; the beta ratio; and SynchFastSlow. The BSR is the proportion of the suppressed EEG (isoelectric) in an epoch, the beta ratio is the log ratio of the power in two empirically derived frequency bands (high- and medium-frequency ranges), and SynchFastSlow is the relative bispectral power in the 40–47 Hz frequency band. The bispectral analysis examines the relationship between the sinusoids at two primary frequencies, f_1 and f_2, and a modulation component of the frequency f_1+f_2.[5] The set of these three frequency components is known as a triplet. The bispectrum can be decomposed to isolate the phase information as bicoherence and the combined magnitude of the members of the triplet as the real triple product. EEG recordings from thousands of patients undergoing anaesthesia with many different anaesthetic techniques were collected by Aspect Medical Systems, together with clinical information related to anaesthetic depth. After processing, a database was created describing the EEG-derived subparameter and the corresponding clinical state (level of unconsciousness). The subparameters were then ranked by their ability to predict a particular clinical condition. The exact weighting of each subparameter is not available from the proprietors. The weighted sum of the subparameters is the BIS number. Thus, BIS is a variable computed using complex methods (but giving a simple quantitative indication of the depth of anaesthesia), and there is no simple mathematical relationship between the parameters that add up to the BIS.

Miller and colleagues[6] have attempted to analyse the contribution of one of the components (SynchFastSlow) to the BIS. The authors obtained EEGs from 39 patients and calculated the simple power spectrum-based parameter PowerFastSlow and the bispectral parameter SynchFastSlow, and correlated them with the state of anaesthesia. Having shown a good correlation, they subsequently plotted the receiver operating characteristic curve for each method and showed that there is good agreement between the two methods. They therefore concluded that bispectral analysis added little to power analysis, and thus may have added little to the interpretation of BIS. This may imply that bispectral analysis is a gimmick or a trick of the trade, and that a simpler form of assessment of the EEG is sufficient to predict the depth of anaesthesia.

However, the results of this study must be interpreted carefully. One of the aims of the study seems to be to determine whether the bispectrum adds any information to the power spectrum. Power spectrum and bispectrum each have their own advantages, and represent two different types of information. The authors compared these second- and third-order parameters by using a Bland and Altman plot. This plot indicates the extent to which the parameters agree but does not show that there is no additional information to be obtained from the bispectrum. The presence of such additional information can only be confirmed by multivariate analysis. The authors should also have applied a test of paired proportions to further clarify the significant concurrence in the two methods. The EEG signals in the non-concurrent cases determined by these methods can be analysed further. The upper and lower limits of agreement should have been calculated for SynchFastSlow *vs* PowerFastSlow and BIS *vs* PowerFastSlow, to determine the degree of agreement and the bias. However, this study has limited data from 39 patients. Furthermore, the authors demonstrate that the bicoherence component of the bispectrum is not related to the state of unconsciousness. However, this does not indicate that the other component, the real triple product of the bispectrum, is equal to the power spectrum, and other contributing factors attributable to the bispectrum cannot be ruled out.

If one argues that the loss of information in the PowerFastSlow is of no consequence in terms of predicting the level of unconsciousness, one should probe the reasons for the limited success of earlier processed EEG variables. This has been related to the fact that, in an EEG signal, the informative content and data association are too complex to be extracted by traditional algorithms. For instance, power spectral analysis quantifies power distribution only as a function of frequency, ignoring phase information. It also makes the assumption that the signal arises from a linear process, thereby ignoring potential interaction between components of the signal that are manifested as phase-coupling, which is a common phenomenon in signals generated from the central nervous system. The performance of such quantitative EEG parameters as an anaesthetic depth monitor suffers because of their sensitivity to specific types of EEG patterns. The higher-order statistical analysis obtained by bispectral analysis is expected to improve the quantification of the change in EEG signal produced by anaesthesia as it has several advantages: it enhances the signal-to-noise ratio for non-Gaussian EEG; it identifies non-linearities in the signal generation process; and it quantifies both power and phase information. Indeed, the BIS number was derived not only on the basis of bispectral analysis but also from two additional subparameters, burst suppression (time domain analysis) and the beta ratio (frequency domain analysis). Under these circumstances, where the higher-order statistical analysis has been performed to quantify changes related to maximum parameters, most readers would find it difficult to appreciate the need for an alternative statistical analysis and that, too, of a lower order.

In addition, not only has the BIS been derived on the basis of a sizeable database, but it also has the advantage of having been tested on a large number of patients. There have been more than 5 000 000 general anaesthetics in which the BIS monitor has been used, out of which a total of 83 episodes have been referred to the manufacturers as cases of possible awareness.[7] In 48 cases, the BIS was found to be greater than 65 at the time of awareness, in 10 cases the BIS was not being used at the time of awareness, and in the remaining cases the cause of the awareness was not conclusively determined.

Should the PowerFastSlow (as suggested by Miller and colleagues)[6] undergo similar evaluation as an independent parameter or after substituting it for the SynchFastSlow component of the BIS? The answer depends upon whether the BIS can be considered to be the ultimate monitor. It is unrealistic to expect a monitor that predicts the probability of awareness to have 100% specificity (no false negatives). One case report describes a patient being aware at a BIS of 47.[8] The BIS is known to be unaffected by nitrous oxide[9] and by ketamine.[10] It has been shown that the BIS is not an accurate measure of depth of anaesthesia when fentanyl with or without propofol[11] or fentanyl and midazolam are used during coronary artery bypass grafting.[12] In addition, it may not predict awareness in reaction to intubation in surgical patients.[13] The BIS has also not been shown to be robust enough when artefactual signals are present. For example, interference with the BIS from pacemakers has been found in patients during cardiac surgery,[14] and has also been found from the use of electric blankets.[15] Large-scale controlled clinical trials designed to determine exactly how effective the BIS monitor is in preventing unintentional intraoperative awareness in surgical patients are necessary, and perhaps going on, and one eagerly awaits the results. Nevertheless, BIS monitoring appears to be generally associated with a low incidence of awareness. Even so, a need to further improve the performance of the BIS monitor cannot be denied. It was suggested by Dr M. M. Todd,[16] in his editorial in 1998, that a skilled engineer might build a device that calculated parameters totally different from the ones used by the Aspect Medical System. He stated that anyone willing to spend the time, effort and money to collect, analyse and correlate this information can construct a device that may perform as well as or better than the BIS. Research with such an objective has been limited. One report has tried to find the relationship between burst suppression and the BIS,[17] while in another report Ortolani and colleagues[18] have attempted to use a neural network technique to obtain a non-proprietary index of the depth of anaesthesia from processed EEG data. Ortolani and colleagues[18] have used as many as 13 EEG variables, including power derived from different frequency ranges of the EEG, their ratio, the suppression ratio, the spectral edge frequency and the median frequency, to derive a scoring system to predict the level of unconsciousness. Their contention was that the BIS may not prove to be the optimal system because part of the information present in the EEG signals is not utilized. Both papers showed that the parameters that were studied correlated well with the BIS in terms of predicting the level of unconsciousness. The paper by Miller and colleagues[6] is yet another attempt to modify the BIS monitor or develop a different monitor. It seems that these papers are an initial step towards further improvement in our techniques of monitoring the depth of anaesthesia. Time will tell whether a monitor can be developed that offers a better assessment of the level of unconsciousness.

Finally, there is growing pressure on Aspect Medical Systems to make public the complete information regarding the workings of this device through a scientific publication. This will not only help to support or refute the contention that Miller and colleagues[6] are so persuasively trying to argue, but will also put an end to the complaints (if any) regarding the publication of articles describing the use of a black box for which the complete details are a trade secret. The secrecy may be related to financial interests, which do not concern practising anaesthetists. However, other information related to the functioning of the monitor, such as the memory function, has also not been disclosed.[19] It is difficult to comprehend such secrecy and any openness shown by the manufacturer will only help to strengthen the confidence of the user.

It is heartening to note that the practice of anaesthesia is evolving on the basis of a scientific approach to improving patient care. The paper by Miller and colleagues[6] should be considered on these principles and is likely to facilitate additional research into the development of neurological monitoring techniques.

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