To BIS or Not to BIS? That Is the Question

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This editorial accompanies two papers (1,2) on the use of the Bispectral Index (BIS) as a sedation index in children. Before discussing the salient elements and findings of these papers, it is instructive to consider what processed electroencephalogram (EEG) monitors actually measure.

As an analogy, consider the dark days before the introduction of pulse oximetry into clinical practice, when clinicians generally used something that might approximate to a four-point scale (pink/slightly blue/dark blue/black) to assess oxygenation. The introduction of pulse oximetry gave a continuous measure of oxygen saturation as a percentage of saturated hemoglobin and quickly became the gold standard for measuring oxygenation, despite the lack of prospective randomized trial evidence of improved outcomes (3). Similarly, we have multiple discontinuous clinical scales for describing sedation levels in adults, including the Observer’s Assessment of Alertness and Sedation (OAAS) and the Ramsay scales. The purpose of processed EEG monitors is to provide a continuous measure that encompasses the full range of sedation levels measured by the discontinuous scales.

Pulse oximetry measures a physiological parameter that most physicians can readily understand (oxygen saturation). In contrast, processed EEG monitors calculate a mathematical abstraction of the electroencephalogram, a concept less familiar and less accessible to the practicing clinician. BIS was derived by empirically estimating the EEG parameters that best predicted OAAS measurements in a large patient and volunteer database of subjects receiving hypnotics and opioids. As a continuous measure that correlates to OAAS measures obtained from subjects receiving hypnotic drugs, BIS may be described as a “probability of state” measure, reflecting the complex nature of consciousness (4).

Being derived from the OAAS, BIS should be expected to correlate well with the OAAS. The correlation would probably be less strong with other rating scales, such as the Ramsay scale, the modified maintenance of wakefulness test (MMWT) scale used in pediatrics, or the University of Michigan sedation scale (UMSS). These latter scales were not part of the database used to develop the BIS monitor, and the original database was entirely constructed from adult EEG data. Normal pediatric EEG differs markedly from adult EEG, displaying more variation than adult EEG (5,6). This may make processed EEG parameters less reliable in children. In general, the electrical activity of the brain changes during growth and development, warranting age-specific considerations and cautious interpretation of EEG data in the pediatric population.

Despite such theoretical concerns, studies suggest that the performance of BIS in pediatric patients older than 6 months of age may be similar to that of adults (7–9). In younger infants, brain maturation and development may render processed EEG measures unreliable. However, McDermott et al. (8) still found a significant correlation between BIS and the UMSS in patients younger than 6 months of age in a small group of patients.

In this issue of Anesthesia & Analgesia, Malviya et al. (1) report on the observed relationship between BIS and two observational measures, the UMSS and MMWT, in children 1 month to 17 years conceptual age. In lieu of clinical guidelines that call for delineation of sedation states, the investigators were particularly interested in the ability of different measures to discriminate conscious from deep sedation. Data from 39 patients were included, comprising repeated measurements (about 8 per individual on average) of sedation indices after unspecified procedures that required sedation/analgesia or general anesthesia. The authors report good correlation between UMSS and BIS (−0.73), indicating reasonable concordance between these discontinuous and continuous scales. This supports the validity of BIS as a pediatric sedation monitor and complements similar reports by this group (10) and others (8). MMWT scores, by contrast, correlated weakly (0.36) with BIS, in contrast to earlier
Given the wide variation in normal pediatric EEG, specific hypotheses should be studied in specific age groups of appropriate size (determined by power analysis). In our view, the recommendation of Malviya et al. (1) that the cutoff for deep sedation in pediatric patients should be 80 requires prospective validation before it is adopted as a clinical guideline. Also in this issue, Sadhasivam et al. (2) adequately address most of the methodological issues raised here and elsewhere (17). They studied a larger group of children ($n = 96$) who varied less in age, and excluded young infants ($<1$ year). Besides the UMSS, these authors incorporated the OAAS as a sedation measure to test the hypothesis that BIS is a valid measure of pediatric sedation depth. BIS was automatically and electronically recorded, and only values immediately (40 s) preceding observational scores were considered for paired-data analyses. A further feature of this report is the distinct consideration of BIS values when the two observers rated the sedation level equally. This eliminates interrater variability (occurring about 50% of the time in the Sadhasivam et al. report (2)), another common limitation of observational scales, and allows for a more accurate assessment of the BIS value across sedation levels. Given observational agreement, Sadhasivam et al. (2) found reasonably good prediction probabilities for BIS and the clinical sedation scores. Prediction probability is a nonparametric statistical measure of association that takes data limitations into account (18). This finding again supports the feasibility of BIS as a pediatric sedation monitor. In addition, BIS values were strong predictors of OAAS and UMSS scores independent of drug regimen, an issue that could not be addressed by Malviya et al. (1). Sadhasivam et al. (2) explicitly excluded children receiving ketamine, a drug that is known to affect BIS in a paradoxical manner (8,19).

Pediatric populations pose particular challenges, especially when delicate information is to be abstracted and traumatic experiences may be involved (20). The utility of BIS to monitor depth of sedation should not be interpreted as suggesting that BIS can substitute for a vigilant, trained anesthesiologist caring for children receiving sedation. Deep sedation should only be administered by trained anesthesia personnel. When nonanesthesiologists sedate children, general anesthesia is induced in up to 35% of patients, and 8% of patients have adverse airway events including desaturation (9).

As investigators with an interest in awareness and memory function during anesthesia, and the interplay between awareness and processed EEG parameters, we welcome the recent interest in pediatric sedation monitoring. It took more than a decade of research to understand the issues involved in adult sedation monitoring. The database in children is relatively sparse.
compared with the adult database. But the same research issues and clinical concerns arise with children as with adults: What is the appropriate clinical response measure to compare to processed EEG? Many still argue that movement is the gold standard (17), but we disagree when it comes to measuring sedation. What are the effects of different drugs? What does a single BIS value mean in different patients?

In adults, BIS monitoring reduces drug usage without jeopardizing primary clinical end-points (13,21). Similar results have been obtained in the pediatric population (22). Brain monitoring facilitates early recovery from anesthesia (13), reduces the risk of awareness in high risk patients (23), and reduces postoperative nausea and vomiting (24). BIS may even provide information about the anesthetic state that relates to the risk of postoperative mortality (25).

To BIS or not to BIS? More generally, should we monitor the EEG intraoperatively or not? We can answer this in adults by asking whether the cost of the technology is reasonable (yes), whether it provides the caregivers with useful information (yes), and do available data suggest the technology influences short-term or long-term outcome (yes). Are the data sufficiently strong in the pediatric population to endorse a similar recommendation? In pediatric patients older than 1 year of age, the technology appears to perform in a similar manner to the adult population but further data are needed to support this conclusion. The results are less convincing for patients in their first year of life. However, in the pediatric population older than 1 year of age, we answer the question posed in our title with a cautious “Yes.”

References