Why Does Bispectral Index Monitoring Not Perform Better?

To the Editor:

We read with great interest the results of the largest Bispectral Index (BIS) monitoring study ever performed, which was published in the October 2012 issue of ANESTHESIOLOGY.¹ No significant difference in intraoperative awareness with explicit recall was detected between BIS and anesthetic concentration protocols (0.08 vs. 0.12%, P = 0.48) in an unselected surgical population of 21,601 patients. Initial multicenter studies suggested that BIS monitoring could reduce the incidence of explicit recall in high-risk surgical patients,² but later studies that compared BIS monitoring with carefully guided dosing schemes with audible alerts for low concentrations of the anesthetic failed to demonstrate such benefit.³,⁴ Now, this negative result was corroborated in a “normal” population (BIS < 60 vs. minimum alveolar concentration > 0.5). What went wrong? Why does BIS monitoring not perform better?

We believe that there are two main reasons. First, the suggested intraoperative “therapeutic window” (BIS 40–60) to guide anesthetic dosing is not optimal for preventing unintended awareness and is most probably dictated by manufacturer’s aspiration to not to prolong awakening after anesthesia. The scientific evidence that BIS should be kept below 60 to prevent awareness is extremely weak if not totally nonexistent. We find it incomprehensible that this fundamental issue is not dealt with in the literature. Every anesthesiologist who has used BIS monitoring knows that BIS level 60 represents a labile “depth of anesthesia,” and even a small surgical or other irritation can lead to arousal and awakening. Deepening anesthesia induces characteristic electroencephalographic changes, labile “depth of anesthesia,” and even a small surgical or other irritation can lead to arousal and awakening. Deepening anesthesia induces characteristic electroencephalographic changes, and lowering the reference range would undoubtedly improve the sensitivity of BIS to prevent awareness despite the wide interpatient variability in its concentration–response curves and partially distinct electroencephalographic effects of different anesthetic agents. Because of the nonlinear behavior of BIS,⁵ keeping it close to 40 is actually relatively easy.

Our recent positron emission tomography imaging study with anesthetized healthy subjects suggests another reason for the poor performance of BIS. The emergence of consciousness after anesthetic-induced unconsciousness, as assessed with a motor response to a spoken command, was found to be associated with activation of deep, primitive brain structures rather than the evolutionary younger neocortex.⁶ Unexpectedly, activation of these central core structures was enough for the arousal and behavioral expression of subjective awareness. Because BIS is based on cortical electroencephalographic measurement (i.e., measuring electrical signals on the surface of the scalp that arise from the brain’s cortical surface), these results help to understand why BIS fails in differentiating the conscious and unconscious states in the subtle transition phase during emergence⁷ and why patient awareness during general anesthesia may not always be detected.


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We also have two minor comments concerning the article by Mashour et al.1 and the accompanied editorial.8 On the basis of the detailed description on page 719, the most important principle of randomization and the randomized controlled trial paradigm may have been breached; in a randomized trial, the investigator should not know the treatment/intervention allocation before patient recruitment. Or have we misunderstood the procedure? In addition, the editorial included a funny flaw: BIS spectroscopy. Surely, we are not able to scope anything with BIS.

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To BIS or Not to BIS

To the Editor:
I read with interest the study by Mashour et al.1 The authors are to be congratulated for having performed this large randomized trial to answer an important question regarding the utility of bispectral index monitor and comparing that to minimum alveolar concentration level alarm system.

There are few points that warrant clarification. First, the author included patients who received total intravenous anesthesia. However, the details of this subgroup of patients were not provided. The method of determining the minimum alveolar concentration level in the no bispectral index total intravenous anesthesia patients, the alarm limits, and the incidence of awareness in these patients were not described.

Second, the inter-rater agreement using Fleiss K statistic for the three blinded assessments of awareness showed fair agreement (0.25). Can the authors comment on the low level of agreement and provide the confidence interval for K?

Third, 36% of patients did not have bispectral index data recorded because of technical issues. While this could provide a third arm for comparison, it may also create some bias. Providers who did not receive an alarm might have decreased vigilance as they could have depended on the alarm system. Adding a third arm of routine care in the design might have provided valuable information.

Finally, it would have been interesting to learn more about the 19 definite awareness cases in this large sample which could help in refining the characteristics of high-risk patients.

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In Reply:
We thank Dr. Myles for his thoughtful comments on our editorial1 and his contribution to the field of anesthesiology in general and comparative effectiveness research (CER) specifically. The points, including the disagreement with our categorization of the discussed trials, are well taken and are representative of a wider discussion about the question of what actually constitutes CER and what methodologies should be used to achieve it.2,3 Although the most commonly used definition in the United States today is that put forth by the Federal Coordinating Council for Comparative Effectiveness Research in 2009,* it can be argued that principles