Depth of Anesthesia

Perhaps the Patient Isn’t a Submarine

The discipline of anesthesiology is awash with metaphors,¹ but none more pervasive and alluring than the idea of “depth-of-anesthesia.” Every working day anesthesiologists constantly adjust anesthetic drugs to try and get the patient to the perfect “depth-of-anesthesia” appropriate for the surgical conditions. In the most literal sense, the patient is analogous to some sort of submarine, entering the state of anesthesia by a discontinuous transition (he or she will “dive under the water”). Then, by changing the anesthetic drug concentrations (equivalent to altering the ballast tanks in the submarine), the patient can be held at various “depths” – analogous to the one-dimensional vertical distances between the submarine and the surface of the water. In this issue of Anesthesiology, the article by Whitlock et al.² asks the question: “How well does the bispectral index (BIS), a putative measure of depth-of-anesthesia, track the effect-site volatile anesthetic concentration during the maintenance phase of anesthesia, in a reasonably large number of patients undergoing clinical anesthesia and surgery?” The study is important because it presents information about the real-life variability of the anesthetic drug concentration-effect relationships. It also implicitly assumes that increasing the anesthetic drug concentration during the maintenance of anesthesia will cause progressive impairment of neurologic function (“depth-of-anesthesia”), which then should be reflected by a decrease in the BIS value.

The authors start by setting out criteria for the rigorous evaluation of electroencephalographically based “depth-of-anesthesia” monitors. It is a development of ideas presented in a previous article by the group.³ In essence they suggest there should be both: (1) a narrow range of electroencephalogram-index values at the point where patients transit between unresponsiveness and responsiveness, and also (2) a steep and consistent gradient in the relationship between anesthetic drug concentrations and putative electroencephalogram-index during the maintenance phase of anesthesia. Unfortunately the presently available monitors do not meet these standards. They tend to produce curves similar to that shown in figure 1B in their paper. The relationship between various quantitative electroencephalographical indices and volatile anesthetic concentrations has been extensively studied previously in small groups of patients, who typically receive strictly controlled, and often slightly artificial, anesthetic regimens.⁴ ⁵ These studies usually concentrate on assessing the ability of the index to separate the awake state from the unresponsive state. Fewer studies have explicitly looked at how reliably the BIS tracks hypnotic drug concentrations at higher doses during the maintenance phase, when the patient is already unresponsive,⁶ but have found similar results to those reported by Whitlock et al. Although there was significant statistical relationship between anesthetic agent concentration and BIS, it was too weak and variable to be clinically useful. These results would come as no surprise to any clinician who uses electroencephalographic monitoring during general anesthesia. In trials where general anesthesia is titrated to a target range of BIS values, the targets are typically achieved only about half the time. In about 10% of patients the BIS value will actually increase as the anesthetic drug concentration increases (see fig. 6C in Whitlock’s paper, and fig. 1 in the paper by Kreuer et al.⁶). One possible explanation of this problem is that the existing electroencephalogram-index algorithms were designed specifically to maximally separate the awake and unresponsive states, with little regard to the higher

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end of the anesthetic dose-response curves. However, perhaps the failure does not lie with the equipment and signal processing, but rather the failure lies with our understanding of the process of general anesthesia. The fact that this study, and others, have failed to find a reasonably consistent relationship might indicate that, over these dose ranges, the patient’s neurologic function is actually not really changing very much in response to the increase in anesthetic concentration; this lack of change is being accurately reflected by the lack of change in the BIS. In essence increasing anesthetic concentration did not cause a decrease in the BIS because: “You can’t further switch off something that is already switched off …”

Arguably the most perceptive definition of “depth-of-anesthesia” is proposed by Shafer and Stanski. They define “depth-of anesthesia” multi-dimensionally as the probability of various responses to various stimuli. By invoking a probability function in the definition, they convert what is intrinsically a binary on-off measure into a pseudocontinuous measure, analogous to “depth” under water. However, anesthetic dose-response curves are often very steep. Invoking Occam’s razor, it would be simpler and perhaps more meaningful to do away with the idea of “depth” and use the metaphor of a household switch-board rather than a submarine; i.e., volatile anesthetics act to close a series of almost binary switches in various subsystems within the nervous system. These multiple dimensions of the general anesthesia syndrome need to be explicitly unbundled. Instead of asking ourselves the somewhat blurred question of “Is the depth-of-anesthesia optimal?” we should be asking ourselves a series of more specific questions that target partially correlated but distinct neurobiological systems that probably should be suppressed during successful general anesthesia. Some of these questions might be:

“Have I switched off the patient’s memory systems?”
“Have I switched off the patient’s consciousness systems?”
“Have I switched off the patient’s noxious arousal systems?”
“Have I switched off the patient’s autonomic responses?”
“Have I switched off the patient’s somatic responses?”
“Have I switched off the patient’s postsurgery hyperalgesic responses?”
“Have I switched off the immune-inflammatory responses?”

Clearly it is very unlikely that the electroencephalogram could directly answer any more than the first two or three questions, which are intuitive for experienced anesthesiologists practicing their craft. However, to achieve scientific progress, we should go beyond trying to find a single one-dimensional monitor that combines all those questions together, instead developing separate monitors that can optimally answer each question individually.

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