Bispectral Index and Detection of Noxious Stimuli

To the Editor:

We congratulate Funcke *et al.*[1] for their work on the validation of various techniques for monitoring nociception. The authors reported that the Analgesia Nociception Index, the Surgical Pleth Index, and pupil diameter are efficient for the detection of noxious stimuli, while the Bispectral Index (BIS) is not a marker of the analgesic level. However, in this study, deep sedation with propofol was used to allow laryngeal mask insertion without opioids or neuromuscular blocking agents, and consequently, all patients required norepinephrine infusion. As reported in table 4,[1] the BIS values varied between (95% CI, 24 to 28) and 31 (95% CI, 28 to 34) before tetanic stimulation or 27 (95% CI, 25 to 29) and 33 (95% CI, 30 to 37) before intracutaneous stimulation. We would like to point out that the BIS level sought by the authors (24 to 37) is lower than the usual recommendations (40 to 60 or 45 to 60). It is therefore possible that tetanic stimulation was not sufficient to provoke electrocortical activation because of the too deep sedation. Let us mention three studies showing a quite different result compared to that of Funcke *et al.* Laryngoscopy induces an increase in BIS value when the patients have a BIS value around 50 before stimulation, BIS variation being inversely proportional to the administered concentration of remifentanil.[2] Similarly, it has been reported that BIS increases in moderately sedated patients who have received a painful stimulus and that this response was blocked by the analgesic or increasing propofol concentrations.[3] The last study showed that BIS increases during moderate and severe noxious stimuli, but the variation was moderate when patients are deeply sedated (BIS < 40).[4] Finally, regarding BIS variation after noxious stimuli, Funcke *et al.* demonstrated that the electrocortical activation after noxious stimuli is abolished during too deep sedation.

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Competing Interests

Dr. Liu and Dr. Chazot are the cofounders of MedSteer (Groslay, France), a company dedicated to creating closed-loop systems for the delivery of anesthetic drugs. Dr. Fischler is the president of the scientific committee of MedSteer.

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In Reply:

We appreciate the interest of Liu *et al.* in our article.[1] This offers the opportunity to put more emphasis on the role of sedation level, displayed by the parameter bispectral index, on analgesic monitoring. As Liu *et al.* pointed out, the patients' Bispectral Index (BIS) values in the study were lower than recommended values during surgical procedures. As they assumed in their letter, these low values are caused by the initial bolus of propofol for induction of general anesthesia and successful placement of the laryngeal mask. Persistence of low BIS values with a standard dosage of propofol of 4 to 5 $mg \cdot kg^{-1} \cdot h^{-1}$ is not unusual when considering that patients were in a stimulus-reduced dark and silent room. The aim of our study was to compare the detection of nociceptive stimuli on different analgesic levels but on the same level of sedation, and accordingly the BIS values were low throughout the whole intervention period. We agree that tetanic stimulation obviously was not sufficient to provoke electrocortical activation in the sense of "arousal" from deep sedation. This is exactly our point: The nociceptive stimulus provoked a significant change in analgesic indices and pupil dilation, but not in BIS values. Furthermore, the extent of the change in analgesic indices and pupil dilation was diminished by an increase of opioid administration (fig. 2).[1] Thus, the Analgesia Nociception Index and Surgical Pleth Index as well as the pupil diameter are proven to reflect the analgesic level. BIS in contrast did not correlate at all with the application of a nociceptive stimulus. Consequently, BIS does not display the analgesic level. Other authors' findings support our conclusion that BIS monitoring is unable to detect and predict stimulation response.[2,3]

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