

## Bispectral Index and Detection of Noxious Stimuli

To the Editor:

We congratulate Funcke *et al.*<sup>1</sup> 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,<sup>1</sup> 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 remifentanyl.<sup>2</sup> 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.<sup>3</sup> 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).<sup>4</sup> Finally, regarding BIS variation after noxious stimuli, Funcke *et al.* demonstrated that the electrocortical activation after noxious stimuli is abolished during too deep sedation.

### Research Support

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### Competing Interests

Dr. Liu and Dr. Chazot are the cofounders of MedSteer (Grosly, 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.<sup>1</sup> 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 · kg<sup>-1</sup> · h<sup>-1</sup> 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).<sup>1</sup> 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.<sup>2,3</sup>

Yet some studies demonstrate a synergy between sedatives and analgesics that causes a significant interaction for the response to tetanic stimulation. In a study published in 2018 by Sabourdin *et al.*,<sup>4</sup> pupillary reflex dilation was more sensitive in detecting a noxious stimulation at BIS levels around 55 than at 25. Sabourdin *et al.* conclude that BIS is displaying the level of cortical inhibition and not nociceptive status. But to a certain extent, BIS monitoring can be able to detect somatic responsiveness.<sup>5</sup> In these situations, BIS reveals secondary information from the noxious stimulus when reaching the cerebral cortex *via* ascending pathways. Thus, it is rather a marker of arousability than measuring the balance between nociception and antinociception. In that regard, the literature that Liu *et al.* reference is not contradictory to our results.

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The underlying study was an investigator-initiated trial and was supported by departmental funds only. The three monitoring devices used were loaned by the companies mentioned throughout the publication.

### Competing Interests

The authors declare no competing interests.

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## Left Uterine Tilt for Cesarean Delivery Significantly Improves Maternal Hemodynamics and Should Not Be Considered Outdated Dogma

*To the Editor:*

We would like to congratulate Lee *et al.*<sup>1</sup> on their excellent study, which challenged medical dogma and demonstrated that with appropriate management of the blood pressure during a spinal anesthetic for a cesarean delivery, left uterine displacement does not affect the acid-base status of the neonate. The study was well-designed and executed; however, we strongly disagree with the authors' interpretation of the data such that "...findings do not support the historical practice and current recommendations for LUD [left uterine displacement] as being essential during elective cesarean delivery to support maternal hemodynamics, prevent spinal-induced maternal hypotension, and maintain neonatal acid–base status in healthy nonlaboring women with uncomplicated pregnancies."<sup>1</sup>

Lee *et al.*<sup>1</sup> found that the lack of left uterine displacement did not impact neonatal acid-base status; however, maternal hemodynamics were negatively affected in the group not receiving left uterine displacement. Maternal blood pressure and cardiac output were both significantly lower in the supine compared to left uterine displacement group, despite the supine group receiving 29% more phenylephrine.<sup>1</sup> Therefore, rather than concluding that left uterine displacement is not necessary, the study actually demonstrates that left uterine displacement is beneficial and does improve maternal hemodynamics significantly.

In addition to the mean outcome differences between groups in the study cohort, it is critically important to consider the relatively rare, but serious adverse events that occur in some individuals after the induction of spinal anesthesia. The study was not adequately powered to detect the influence of the supine position on the incidence of events such as reflex bradycardia and cardiovascular collapse. Even in this small cohort, however, there were some women in whom the lack of left uterine displacement appeared to have a profound impact. One subject in the supine group had a clinically significant drop in blood pressure to 44/22 mmHg, and the lowest base excess was in the supine group. There was also the one patient in the left uterine displacement group who became symptomatic with a systolic blood pressure decrease from 122 to 75 mmHg while lying supine before her anesthetic. Supine hypotensive syndrome occurs in approximately 8% of women at term; and even if left uterine displacement does not benefit the entire study cohort, these individuals may benefit from left uterine displacement.<sup>2</sup> Consistent with this concern, Lee *et al.* previously showed that although cardiac output only decreased 5% on average in the patients tilted less than 15° compared to when tilted at 15° or greater, cardiac output decreased by 20% in a subset of patients in the less tilted group.<sup>3</sup>

On the surface, the data from Lee *et al.*<sup>1</sup> suggests that left uterine displacement may not be essential; however, a deeper