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CORRESPONDENCE

Peri-operative multimodal monitoring: a real need or a luxury?

Zahra Moaiyeri[1] · Flávia Duarte[2] · Massimo Lamperti[1] · Francisco A Lobo[1]

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Abstract
The present case of a patient with several co-morbidities undergoing complex vitrectomy under peribulbar block and sedation with Target Controlled Infusion (TCI of propofol and dexmedetomidine with EEG and Analgesia Nociception Index (ANI) monitoring illustrates the benefits of multimodal monitoring to differentiate the effect of hypnotic and antinociceptive drugs.It is highlighted the delta-alpha electroencephalographic pattern showing adequate sedation, the beta arousal pattern in the EEG concommitant to decrease in the ANI translating insufficient anti-nociception.

Keywords Multimodal anesthesia · Multimodal monitoring · Electroencephalogram · Analgesia Nociception index (ANI)

To the editor:

A 58-year-old male patient with past medical history of arterial hypertension, coronary artery disease, previous ischemic stroke on the territory of the left middle cerebral artery, diabetes mellitus, obesity and previous bariatric surgery was presented for complex vitrectomy with an estimated duration of 160 min. The patient received a peribulbar block and sedation. Sedation was achieved with Target Controlled Infusion of propofol and dexmedetomidine. The electroencephalogram (EEG) was monitored with a 4-channel frontal montage at F7-Fp1-Fp2-F8, reference electrode at AFz and ground electrode at Fpz using the SedLine® monitor incorporated in the Root® monitoring platform (Masimo, Irvine, CA, USA). In addition, the Analgesia-Nociception Index® (ANI, MDoloris Medical Systems, Lille, France) was monitored using the proprietary module available for the Root monitor.

Patient achieved initially a level − 4 of the Richmond Agitation-Sedation Scale [1] with a plasmatic target concentration of 1.2 µg/mL of propofol (Marsh model [2, 3]) and an effect-site target concentration of 0.6 ηg/mL of dexmedetomidine (Hannivoort model [4]). The EEG showed a mix of 10 and 12 Hz spindles with some delta waves, with a peak-max phase coupling pattern [5, 6]. A retrobulbar block was then performed with injection of a volume of 6 mL of a mixture of lidocaine 1% and bupivacaine 0.25% with no reaction during the injection.

After the retrobulbar injection, the ANI increased to 95 andthere was a decrease in the alpha power in the EEG with alpha predominant spindles around 12 Hz in consequence, the target concentration of dexmedetomidine was decreased to 0.3 ηg/mL.

Incision occurred 8 min after the block, no hemodynamic changes and movement were noticed but the patient briefly groaned. Simultaneously, the ANI decreased from 88 to 42 and the EEG showed an increase in the beta power with increase in the Patient State Index (PSI). After intravenous administration of 10 µg of fentanyl and increase of the target concentration of dexmedetomidine to 0.6 ηg/mL, the ANI increased to 84 and became stable between 92 and 82 until the end of the procedure ;the initial alpha/delta pattern gradually appeared again, allowing to decrease the target concentration of dexmedetomidine to 0.3 ηg/mL until the end of the surgerywhile the propofol infusion was always kept at a plasmatic target concentration of 1.2 µg/mL. (Figures 1 and 2). The PSI was always above 50, the upper limit of the optimal hypnotic state for general anesthesia and burst suppression was not detected during the entire case.

✉ Francisco A Lobo
francisco.lobo@me.com

[1] Anesthesiology Institute, Cleveland Clinic Abu Dhabi, Abu Dhabi, UAE

[2] Serviço de Anestesiologia, Hospital Garcia de Orta, Almada, Portugal

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1 Discussion

Perioperative multimodal monitoring constitutes an essential cornerstone of the modern practice of balanced general anesthesia and sedation, optimizing pharmacokinetic and pharmacodynamic interactions between antinociceptive and hypnotic drugs acting in different neural pathways by distinct mechanisms [7], eventually combined with peripheral nerve blocks [8]. A multimodal strategy with close and individualized dosing titration is particularly important in patients with significant co-morbidities to avoid exposure to unnecessary high doses of drugs and to decrease the incidence of deleterious side effects.

EEG monitoring during anesthesia and sedation has been advocated as an important tool, allowing optimization of drug dosing and detecting and predicting neurological complications [9–14]. Different electroencephalographic signatures of anesthetic drugs have been described [9], including spectral changes associated with decrease in drug delivery by infusion pump malfunction [15], related with cognitive performance [16], dynamic changes in the EEG during transitions between loss and recovery of consciousness [17] and general interpretation of EEG spectrograms [9, 14, 18]. In addition, noxious stimulation may have profound effects in the EEG, inducing three possible different changes: beta arousal, paradoxal delta arousal and alpha dropout [19].

Quantification of nociception in patients under anesthesia has been based on the physiological responses to the noxious stimulation and to surgical stress, particularly on the effects on the Autonomous Nervous System (20–21). Heart rate variability, reflecting the balance between sympathetic and parasympathetic activity [22], has been used for that purpose and constitutes the single parameter used to calculate the ANI [21, 23]. ANI is a dimensionless number varying from 0 to 100 where higher ANI values reflect higher parasympathetic activity and corresponding to less nociception [24] and has been shown to be superior in detecting painful stimulation compared to heart rate and mean arterial pressure [25] and to be affected by antinociceptive drugs like opioids [26] and regional anesthesia (27–28). ANI has also been studied in awake or sedated patients on spontaneous ventilation suggesting that patients totally or partially conscious may benefit from its use and that mechanical ventilation is not an absolute requirement for heart rate variability processing by ANI monitor [29].

Of our knowledge, there is no reported direct effect of antinociceptive doses of dexmedetomidine on ANI. Antinociceptive effect of dexmedetomidine is mainly mediated by the activation of inhibitory interneurons synapsing in the dorsal horn of the spinal cord (30–31) and by a dose-dependent decrease in the arousal level through a decrease in presynaptic release of norepinephrine from neurons projecting from the locus coeruleus onto the basal forebrain, thalamic intralaminar nucleus, preoptic area of the hypothalamus and to the cortex [32–34]. Despite the highly selective alpha-2 agonist effect of dexmedetomidine, it appears that low doses as those used in this report are not affecting the cardiac electrophysiology and the heart rate variability in particular independently of nociceptive stimulation [35–37].

The present case provides important information regarding the different electroencephalographic signatures of sedation and nociception in addition to the changes in the ANI:

- Initially, the alpha-delta pattern and the mixed 10 Hz and sleep spindles were the result of the combination of propofol and dexmedetomidine [9, 14], with the shorter spindles arising from the effect of dexmedetomidine [38].
- The appearance of the beta arousal pattern after the incision was interpreted as the result of insufficient antinociception; this sudden and brief increase in the beta power disappeared after administration of a very small dose of fentanyl and an increase in the target concentration of dexmedetomidine, resuming to the alpha-delta pattern.
- The ANI increased after the block, had a significant decrease after the incision and increased again after the administration of fentanyl and increase in the dose of dexmedetomidine. Remarkably, there were no changes in the blood pressure and in the heart rate following the incision (Fig. 3) in agreement with Funcke et al. [25].

These changes in the EEG and in the ANI were globally translating an insufficient anti-nociception due to a short time between the block installation and the surgical incision and to the decrease in the dose of dexmedetomidine. The following sustained high values of ANI were compatible with a full installed block allowing to decrease the dose of dexmedetomidine. The propofol target concentration was not changed as only the nociception-antinociception balance was shown to be inappropriate.

Other interesting findings are the low voltage of the EEG signal (optimal scale of 3 μV/mm), the higher power in the different bandwidths of the EEG on the left side, both compatible with a pre-existing pathological brain and the past medical history of a left hemisphere stroke and the absence of burst suppression which seems to be a risk factor for postoperative neurocognitive disorders particularly in fragile brains (39–40).

In conclusion, this case report shows how multimodal monitoring with EEG and processed heart rate variability may help to understand the insufficient balance between anesthetic consciousness depression and antinociception, allowing to optimize drug dosing schemes accordingly to

Fig. 1
Screenshot of Root Monitor
From above to the bottom, 2 channels of EEG, the PSI trend, the spectrogram, the average ANI trend and the instant ANI trend.
Black box shows the alpha -delta pattern after starting sedation with TCI of propofol and dexmedetomidine, with alpha band more powerful on the left side.
Blue box shows the beta arousal following the incision, with the increase in the power of beta activity, again more visible on the left side.
White box shows the disappearance of activity in the beta and a decrease in the alpha bandwidths as the result of the increase of target concentration of dexmedetomidine.
Magenta box shows the alpha-delta pattern more visible on the left side after the decrease of target concentration of dexmedetomidine.
The red arrow indicates the increase in the average ANI after the incision.
The green arrow shows the decrease in the ANI after the incision. The purple arrow shows the increase in the ANI after the increase in the concentration of dexmedetomidine to 0.6 ηg/mL.

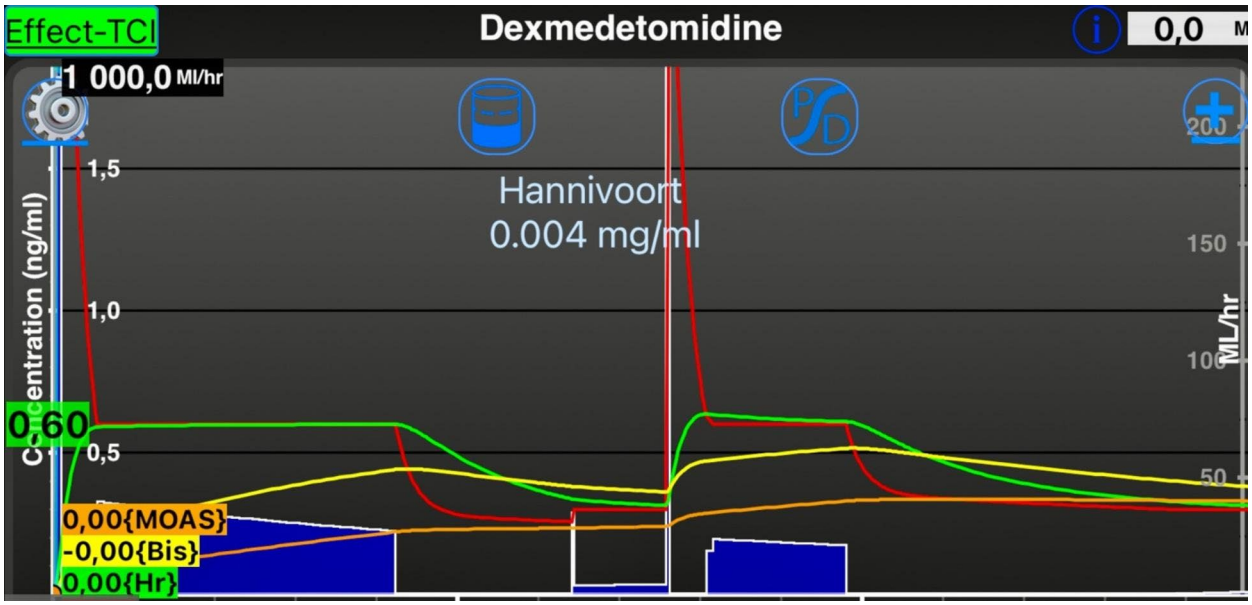

Fig. 2
Simulation with TivatrainerX (https://www.tivatrainerx.com) of the infusion of dexmedetomidine using the Hannivoort model. Green line represents the predicted plasmatic concentration. The red line represents the effect-site concentration. The orange line represents the Modified Observer's Assessment of Alertness/Sedation scale (MOAA/S) predicted by the model. The yellow line represents the Bispectral Index (BIS) values predicted by the model. The blue bar represents the infusion rate.

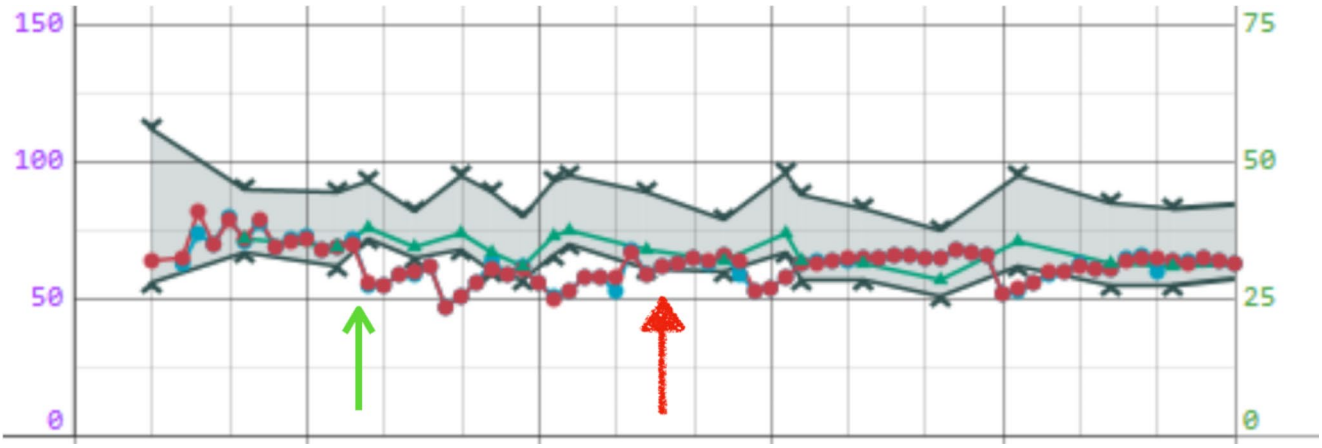

Fig. 3
Trends of heart rate and blood pressure.
Green arrow – retrobulbar block.
Red arrow – incision.

which component is being affected. As we suggested before [15], as the number of monitors incorporating the display of the EEG spectrogram increases simultaneously with the number of monitors intended to evaluate intraoperative nociception, there should be extra efforts in the development of educational and training resources to improve the knowledge of clinicians to interpreter raw EEG and EEG spectrogram images, integrating with other physiological variables and, potentially, leading to an improvement in patient's outcomes.

References

1. Ely EW, Truman B, Shintani A, Thomason JW, et al. Monitoring sedation status over time in ICU patients: reliability and validity of the Richmond Agitation-Sedation Scale (RASS). JAMA. 2003;289(22):2983–91. doi:https://doi.org/10.1001/jama.289.22.2983.
2. Marsh BJ, Morton NS, White M, Kenny GN. A computer controlled infusion of propofol for induction and maintenance of anaesthesia in children. Can J Anaesth. 1990;37(4 Pt 2):97.
3. Marsh B, White M, Morton N, Kenny GN. Pharmacokinetic model driven infusion of propofol in children. Br J Anaesth. 1991;67(1):41–8. doi:https://doi.org/10.1093/bja/67.1.41.
4. Vandemoortele O, Hannivoort LN, Vanhoorebeeck F, et al. General Purpose Pharmacokinetic-Pharmacodynamic

Models for Target-Controlled Infusion of Anaesthetic Drugs: A Narrative Review. J Clin Med. 2022;11(9):2487. doi:https://doi.org/10.3390/jcm11092487.
5. Purdon PL, Pierce ET, Mukamel EA, et al. Electroencephalogram signatures of loss and recovery of consciousness from propofol. Proc Natl Acad Sci U S A. 2013;110(12):E1142-51. doi:https://doi.org/10.1073/pnas.1221180110.
6. Akeju O, Kim SE, Vazquez R, et al. Spatiotemporal Dynamics of Dexmedetomidine-Induced Electroencephalogram Oscillations. PLoS ONE. 2016;11(10):e0163431. doi:https://doi.org/10.1371/journal.pone.0163431.
7. Brown EN, Pavone KJ, Naranjo M. Multimodal General Anesthesia: Theory and Practice. Anesth Analg. 2018;127(5):1246–58. doi:https://doi.org/10.1213/ANE.0000000000003668.
8. Kumar K, Kirksey MA, Duong S, Wu CL. A Review of Opioid-Sparing Modalities in Perioperative Pain Management: Methods to Decrease Opioid Use Postoperatively. Anesth Analg. 2017;125(5):1749–60. doi:https://doi.org/10.1213/ANE.0000000000002497.
9. Purdon PL, Sampson A, Pavone KJ, Brown EN. Clinical Electroencephalography for Anesthesiologists: Part I: Background and Basic Signatures. Anesthesiology. 2015;123(4):937–60. doi:https://doi.org/10.1097/ALN.0000000000000841.
10. Montupil J, Defresne A, Bonhomme V. The Raw and Processed Electroencephalogram as a Monitoring and Diagnostic Tool. J Cardiothorac Vasc Anesth. 2019;33(Suppl 1):3–10. doi:https://doi.org/10.1053/j.jvca.2019.03.038.
11. Li Y, Bohringer C, Liu H. Double standard: why electrocardiogram is standard care while electroencephalogram is not? Curr Opin Anaesthesiol. 2020;33(5):626–32. doi:https://doi.org/10.1097/ACO.0000000000000902.
12. Yang S, Xiao W, Wu H, et al. Management Based on Multimodal Brain Monitoring May Improve Functional Connectivity and Post-operative Neurocognition in Elderly Patients Undergoing Spinal Surgery. Front Aging Neurosci. 2021;13:705287. doi:https://doi.org/10.3389/fnagi.2021.705287.
13. Xu N, Li LX, Wang TL, et al. Processed Multiparameter Electroencephalogram-Guided General Anesthesia Management Can Reduce Postoperative Delirium Following Carotid Endarterectomy: A Randomized Clinical Trial. Front Neurol. 2021;12:666814. doi:https://doi.org/10.3389/fneur.2021.666814.
14. Lobo FA, Saraiva AP, Nardiello I, Brandão J, et al. Electroencephalogram monitoring in anestesia practice. Curr Anesthesiol Rep 2021; 11:169 – 80. doi: https://doi.org/10.1007/s40140-021-00461-6.
15. Lobo FA, Vacas S, Naranjo M. Loss of spectral alpha power during spine surgery: what could be wrong? J Clin Monit Comput. 2021;35(6):1531–33. doi:https://doi.org/10.1007/s10877-021-00720-1.
16. Hesse S, Kreuzer M, Hight D, Gaskell A, et al. Association of electroencephalogram trajectories during emergence from anaesthesia with delirium in the postanaesthesia care unit: an early sign of postoperative complications. Br J Anaesth. 2019;122(5):622–34. doi:https://doi.org/10.1016/j.bja.2018.09.016.
17. Kreuzer M, Kiel T, Ernst L, Lipp M, et al. Evaluation of Anesthetic Specific EEG Dynamics during State Transitions between Loss and Return of Responsiveness. Brain Sci. 2021;12(1):37. doi:https://doi.org/10.3390/brainsci12010037.
18. Ng MC, Jing J, Westover MB. A Primer on EEG Spectrograms. J Clin Neurophysiol.2022; 1;39(3):177 – 83. doi: https://doi.org/10.1097/WNP.0000000000000736.
19. García PS, Kreuzer M, Hight D, Sleigh JW. Effects of noxious stimulation on the electroencephalogram during general anaesthesia: a narrative review and approach to analgesic titration. Br J Anaesth. 2021;126(2):445–57. doi:https://doi.org/10.1016/j.bja.2020.10.036.
20. Guignard B. Monitoring analgesia. Best Pract Res Clin Anaesthesiol. 2006;20(1):161–80. doi:https://doi.org/10.1016/j.bpa.2005.09.002.
21. Ledowski T. Objective monitoring of nociception: a review of current commercial solutions. Br J Anaesth. 2019;123(2):e312–21. doi:https://doi.org/10.1016/j.bja.2019.03.024.
22. Heart rate variability. : standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Circulation. 1996;93(5):1043–65.
23. Logier R, Jeanne M, De Jonckheere J, et al. PhysioDoloris: a monitoring device for analgesia / nociception balance evaluation using heart rate variability analysis. Annu Int Conf IEEE Eng Med Biol Soc. 2010;2010:1194–7. doi:https://doi.org/10.1109/IEMBS.2010.5625971.
24. Jeanne M, Clément C, De Jonckheere J, et al. Variations of the analgesia nociception index during general anaesthesia for laparoscopic abdominal surgery. J Clin Monit Comput. 2012;26(4):289–94. doi:https://doi.org/10.1007/s10877-012-9354-0.
25. Funcke S, Sauerlaender S, Pinnschmidt HO, et al. Validation of Innovative Techniques for Monitoring Nociception during General Anesthesia: A Clinical Study Using Tetanic and Intracutaneous Electrical Stimulation. Anesthesiology.2017;127(2):272 – 83. doi:https://doi.org/10.1097/ALN.0000000000001670.
26. Susano MJ, Vide S, Ferreira AD, Amorim P. Effects of varying remifentanil concentrations on Analgesia Nociception Index® under propofol: an observational study. J Clin Monit Comput. 2021;35(1):199–205. doi:https://doi.org/10.1007/s10877-020-00457-3.
27. Migeon A, Desgranges FP, Chassard D, et al. Pupillary reflex dilatation and analgesia nociception index monitoring to assess the effectiveness of regional anesthesia in children anesthetised with sevoflurane. Paediatr Anaesth. 2013;23(12):1160–5. doi:https://doi.org/10.1111/pan.12243.
28. Dundar N, Kus A, Gurkan Y, et al. Analgesia nociception index (ANI) monitoring in patients with thoracic paravertebral block: a randomized controlled study. J Clin Monit Comput. 2018 Jun;32(3):481–86. doi: https://doi.org/10.1007/s10877-017-0036-9.
29. Baroni DA, Abreu LG, Paiva SM, Costa LR. Comparison between Analgesia Nociception Index (ANI) and self-reported measures for diagnosis pain in conscious individuals: a systematic review and meta-analysis. Sci Rep. 2022;12(1):2862. doi:https://doi.org/10.1038/s41598-022-06993-z.
30. Li R, Qi F, Zhang J, et al. Antinociceptive effects of dexmedetomidine via spinal substance P and CGRP. Transl Neurosci. 2015;6(1):259–64. doi:https://doi.org/10.1515/tnsci-2015-0028.
31. Hunter JC, Fontana DJ, Hedley LR, et al. Assessment of the role of alpha2-adrenoceptor subtypes in the antinociceptive, sedative and hypothermic action of dexmedetomidine in transgenic mice. Br J Pharmacol. 1997;122(7):1339–44. doi:https://doi.org/10.1038/sj.bjp.0701520.
32. Nelson LE, Lu J, Guo T, et al. The alpha2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. Anesthesiology. 2003;98(2):428–36. doi:https://doi.org/10.1097/00000542-200302000-00024.
33. Nelson LE, Guo TZ, Lu J, et al. The sedative component of anesthesia is mediated by GABA(A) receptors in an endogenous sleep pathway. Nat Neurosci. 2002;5(10):979–84. doi:https://doi.org/10.1038/nn913.
34. Brown EN, Purdon PL, Van Dort CJ. General anesthesia and altered states of arousal: a systems neuroscience analysis. Annu Rev Neurosci. 2011;34:601–28. doi:https://doi.org/10.1146/annurev-neuro-060909-153200.

35. Shin S, Lee JW, Kim SH, et al. Heart rate variability dynamics during controlled hypotension with nicardipine, remifentanil and dexmedetomidine. Acta Anaesthesiol Scand. 2014;58(2):168–76. doi:https://doi.org/10.1111/aas.12233.
36. Tan C, Yan S, Shen J, et al. Effects of dexmedetomidine on cardiac electrophysiology in patients undergoing general anesthesia during perioperative period: a randomized controlled trial. BMC Anesthesiol. 2022;22(1):27. doi:https://doi.org/10.1186/s12871-022-01811-5.
37. Tarvainen MP, Georgiadis S, Lipponen JA, et al. Analysis of heart rate variability dynamics during propofol and dexmedetomidine anesthesia. Annu Int Conf IEEE Eng Med Biol Soc. 2010; 2010:1634-7. doi: https://doi.org/10.1109/IEMBS.2010.5626878.
38. Ferenets R, Lipping T, Suominen P, Turunen J, et al. Comparison of the properties of EEG spindles in sleep and propofol anesthesia. Conf IEEE Eng Med Biol Soc. 2006; 2006:635-9. doi: https://doi.org/10.1109/IEMBS.2006.259909.
39. Lobo FA, Vacas S, Rossetti A, Robba C, et al. Does electroencephalographic burst suppression still play a role in the perioperative setting? Best Pract Res Clin Anesthesiol. 2021;35(2):159–69. doi:https://doi.org/10.1016/j.bpa.2020.10.007.
40. Rasulo FA, Hopkins P, Lobo FA, Pandin P, et al. Processed Electroencephalogram-based monitoring to guide sedation in critically ill adult patients: recommendations from an international expert panel-based consensus. Neurocrit Care. 2022 Jul 27. doi: https://doi.org/10.1007/s12028-022-01565-5. Online ahead of print.