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Reading beyond quantitative electroencephalography-based indices: A case of erroneously high Entropy values during ophthalmic surgery

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Running Title: ERRONEOUSLY HIGH ENTROPY VALUES

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- Letter to the Editor -

Maintenance of an adequate depth of anesthesia (DoA) is important among patients undergoing general anesthesia. Quantitative electroencephalography (EEG)-based monitors, such as the bispectral (BIS) index and Entropy, have been established to assess DoA. Nevertheless, these measures can be affected by various factors and the processed numerical output can often be misleading; hence, caution is required when interpreting quantitative EEG-based indices. Here, we report a case of abnormally high Entropy values during ophthalmic surgery with no evidence of intraoperative awareness.

A 61-year-old female patient was scheduled for repair of retinal detachment. Monitoring systems including electrocardiography, noninvasive blood pressure testing, pulse oximetry, end-tidal carbon dioxide measurement, an Entropy™ monitor (GE Healthcare, Finland), and a neuromuscular transmission (NMT) monitor (E-NMT-01; GE Healthcare, Finland) were used. General anesthesia was induced with intravenous injection of fentanyl (75 μg), lidocaine (100 mg), propofol under a target-controlled infusion system (Fresenius Orchestra Primea; Fresenius Kabi AG, Germany) (effect-site concentration [Ce] of 4.0 μg/ml) and rocuronium (40 mg); and maintained with a propofol Ce of 3.0 μg/ml and rocuronium (20 mg/h) initially. Yet during the procedure, entropy values were extremely high with response entropy (RE) values of > 90 and state entropy (SE) values between 80–90. The count of train-of-four of NMT monitor was 0. Assuming inadequate DoA, we titrated propofol Ce at 3.5 mcg/mL and administered sevoflurane at 0.5 minimal alveolar concentration. After we had titrated the anesthetic doses to deepen the DoA, the
Entropy values remained abnormally high while there were no clinical signs of inadequate DoA, such as tachycardia or hypertension. Besides, the raw EEG waveform on the monitor changed from ‘fuzzy’ high frequency beta and gamma waves before anesthetic induction to slow frequency waves of sleep spindles (Fig. 1) during anesthetic maintenance. Meanwhile, the RE values were still > 90 and SE values were within 80-90 even though the patient had lost consciousness with the change in raw EEG waveform. Being certain that the patient was adequately anesthetized, we discontinued the use of sevoflurane. The operation was completed uneventfully and the patient recovered well with no memory of intraoperative awareness.

This case study demonstrates the importance of real-time examination of the raw EEG wave rather than relying solely on quantitative EEG-derived indices. Despite the common use of quantitative EEG-based monitors in assessing DoA, values shown on the monitors can potentially be misleading; for instance, in circumstances with elevated electrode impedance caused by erroneous placement or reduced adherence, low frequency electromyography (EMG) signals being misinterpreted as high frequency EEG signals, iatrogenic movement of limbs, usage of strong vibration producing instruments, interference from electrical equipments such as electric scalpels, electro-cautery, or thermal blankets, and pathologic EEG [1,2,3]. Hypothermia and hypoglycemia have also been found to alter EEG based indices [3]. In addition, the performance of an EEG-based monitor will not be necessarily the same as other models and the model of EEG-based monitor influence the interpretation of the results [3].

Common causes for erroneously high Entropy values during ophthalmic surgery include electro-cautery, electro-oculographic, and electromyographic activity. Alternatively, the surgeon’s hand on the patient’s frontal region where the entropy sensing lead is placed may affect the EMG reading and indirectly affect the Entropy values. However, throughout the reported operation, both RE and SE values remained above 80 despite temporary cessation of electro-cautery.
Meanwhile, the difference between RE and SE values was less than 8 and the count of train-of-four of NMT monitor was 0 – indicating that neither electro-oculographic nor electromyographic activity was the cause of elevated Entropy values in this case. All these measures suggested that the aforementioned common causes of falsely elevated Entropy values during ophthalmic surgery were not the culprit in this case. Moreover, the particular Entropy monitor used in our case was presumed to be functioning normally as the model did not show erroneous results in other patients.

The calculating algorithm of Entropy is mathematical normalization of the overall frequency range of values between 1 (maximum irregularity) and 0 (complete regularity). The theoretical assumption is that irregularity in the EEG signal decreases under anesthesia [1]. In our case, that the EEG signals revealed randomness in wavelength and amplitude from general anesthesia induction to emergence might contribute to erroneously high Entropy values. On the other hand, there are 5-10% of the population with genetically-determined EEG variant whose EEG-based index does not coincide with the clinical state of sedation although it is not associated with any cerebral dysfunction [3]. However, we were unable to know whether our patient have the genetic EEG variation or not.

As BIS and Entropy values are calculated using different algorithms, concomitantly recorded BIS and Entropy values may occasionally show discordant trends during general anesthesia. Aho et al. [4] reported that disagreement between BIS and Entropy values occurred in 11% of the analyzed concurrent pairs. Pilge et al. [2] also reported that SE showed more false classifications of the clinical state at transition when compared with the BIS index (14% versus 9%). We do not intend to claim that one index is superior to the other, but instead whenever discrepancy exists between EEG-based indices and the actual clinical condition, applying two monitoring devices with different EEG algorithms concurrently may provide a more accurate assessment. In addition, as Akavipat et al. [5] suggested that postauricular placement of a BIS electrode can be a practical alternative to
frontal lobe placement during neurosurgery, we support the use of this modality during ophthalmic surgery.

Until now, we still did not know the causing factors of erroneously high Entropy values in our case exactly. However, from this case, we cannot overemphasize the importance of interpreting the raw EEG wave and considering the patient’s clinical condition rather than relying solely on the quantitative EEG-based indices in assuming an inadequate depth of anesthesia. We suggest that employing two EEG-based monitors with different algorithms may provide more accurate assessment when numerical data conflict with the clinical condition. Moreover, we recommend the posterior auricular placement of the EEG sensing electrode as a practical alternative during ophthalmic surgery.
References


Fig. 1. The monitor showed RE and SE values of 100 and 92, respectively. The EEG wave revealed sleep spindles throughout the trace with a consistent and repetitive slow wave background. Vital signs were stable (RE, response entropy; SE, state entropy; EEG, electroencephalography).