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Entropy values are closely related to the degree of neuromuscular block during desflurane anesthesia: a case report

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Abstract

The Entropy™ module and bispectral index (BIS) depth-of-anesthesia monitors have been shown to be influenced by electromyographic (EMG) activity. The increase in entropy and BIS values is most likely caused by increased EMG activity and a higher level of consciousness. A strong EMG activity can increase entropy and BIS values because it is impossible to separate electroencephalography (EEG) from EMG, and this results from their overlapping power spectra. Thus, the entropy module may be more affected by EMG compared with the BIS module because it has more overlap with the power spectra of EEG and EMG. Several studies have suggested that EMG activity is most likely to increase, especially as it relates to the level of total intravenous anesthesia without a muscle relaxant or an insufficient analgesic level, which results in falsely increased entropy values. We present the case of a patient whose entropy values were falsely elevated by increased EMG activity resulting from light neuromuscular block or nociceptive stimuli during surgery even when undergoing desflurane anesthesia. This was closely related to the change in the neuromuscular block level and it was influenced by the degree of analgesia and the remifentanil infusion rate.

Keywords

Consciousness monitors, electroencephalography, electromyography, inhalational anesthetics, neuromuscular blockade, spectral entropy

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Introduction

The Entropy™ module is an electroencephalography (EEG)-based modality to monitor the depth of anesthesia, and it is composed of two parameters: state entropy (SE) and response entropy (RE). SE reflects the hypnotic level of the patient by mainly analyzing the power spectrum (the frequency range from 0.8 Hz to 32 Hz) of electroencephalography (EEG), while RE covers the power spectra (the frequency range from 0.8 Hz to 47 Hz) of both EEG and electromyography (EMG). Because of the overlapping power spectra of EEG and EMG in the frequency range of 10 to 50 Hz, whenever strong EMG activity is present, it is impossible to separate EEG from EMG, which can cause an increase in entropy values.[1,2] An increase in entropy indices or the bispectral index (BIS) is often caused by increased EMG activity.[3,4] The Entropy™ module may be more affected by EMG more compared with BIS, which is mainly influenced by EEG.[5]

The EMG activity is most likely to increase especially the level of total intravenous anesthesia using a low dose of propofol and remifentanil without a muscle relaxant,[1,3,6] which means that the EMG activity is associated with a neuromuscular blockade and nociceptive stimuli or noxious pain as well as the hypnotic level.[3]

We describe the case of a patient in whom entropy values were falsely elevated by increased EMG activity that resulted from light neuromuscular block even when the patient underwent desflurane anesthesia. This was closely related to the change in the neuromuscular block level and it was also influenced by the degree of analgesia and the remifentanil infusion rate. To the best of our knowledge, there has been no report that has described a long-lasting increase of in entropy values resulting from increased EMG activity during inhalational anesthesia.

Case report

A 57-year-old man (174 cm, 65 kg) with a left femur neck and intertrochanteric fracture and pelvic bone fracture underwent surgical correction of the fractures. Entropy™ module monitoring (M-Entropy S/5 plug-in module, Datex-Ohmeda, Helsinki, Finland) was used to ensure an adequate depth of anesthetic. Anesthesia was induced using 140 mg of propofol and 50 mg of rocuronium, and it was maintained using desflurane (5%–6%) and remifentanil (0.02–0.08 μg/kg/minute).

Seventy-five minutes after the induction of anesthesia, a sudden increase in the entropy indices up to 85 for SE and 95 for RE was noticed. Thereafter, despite an adjustment of desflurane up to 7% to 8%, SE and RE generally remained above 80 for 100 minutes throughout the main procedure with some fluctuations in accordance with the degree of surgical stimulation. We confirmed that the Entropy™ sensor was correctly placed on the patient's forehead, and the sensor, which was re-checked, passed with normal results. Until this time, additional rocuronium had not been administered since anesthesia induction, and thus, we suspected that the increase in SE/RE may have resulted from increased EMG activity, although the patient did not move during surgery. After 10 mg of rocuronium was injected (Figure 1, the first red arrow), SE/RE dramatically decreased to 30 to 40. At this time, train-of-four (TOF) monitoring (M-NMT Mechanosensor™, Datex-Ohmeda, Helsinki, Finland) was started in the right adductor pollicis and the TOF ratio was 10. About 45 minutes later, a TOF ratio reached 70 and SE and RE also increased to 70 to 80. SE/RE returned to above 80 for about 30 minutes. After a second injection of 10 mg of rocuronium (Figure 1, the second red arrow), SE/RE suddenly decreased to 30 to 40. About 20 minutes

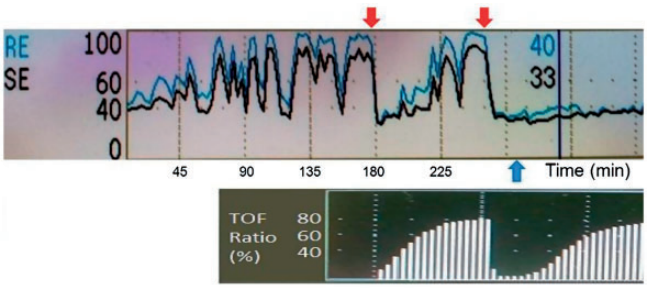

Figure 1. The change in entropy indices and train-of-four (TOF) ratio values during the surgery. Red arrows indicate an injection of 10 mg of rocuronium. A blue arrow indicates the adjustment of the remifentanil infusion rate from 0.08 to 0.12 μg/kg/minute. RE, response entropy; SE, state entropy; Time, the elapsed time from anesthesia induction.

later, the patient's blood pressure exceeded 150/90 mmHg and his heart rate increased to 110 beats/minute. Thus, the remifentanil infusion rate was adjusted from 0.08 to 0.12 μg/kg/minute (Figure 1, blue arrow). Thereafter, SE/RE did not increase by more than 50, even though the TOF ratio increased to above 70 and no more rocuronium was injected until the end of surgery.

The patient's blood pressure (systolic pressure range, 100–145 mmHg; diastolic pressure range, 55–80 mmHg), heart rate (range, 73–101 beats/minute), body temperature, and oxygen saturation maintained at stable levels, suggesting an adequate depth of anesthesia during the rest of the surgery. Total anesthesia time was about 7 hours and intraoperative fluid balance was adequate. The patient did not complain of any intraoperative recall after the surgery.

Written informed consent was obtained from the patient to publish the details of his case. Ethics approval from the local ethics committee was not required because this case was based on routine clinical care using general anesthesia and it did not involve a human study.

The correlation between entropy indices and the TOF ratio using Pearson's correlation test was studied off-line after the patient's surgery. A two tailed P-value of <0.05 was considered statistically significant. In the period between the first rocuronium administration and increasing the remifentanil dose (180–275 minutes, the first arrow to the blue arrow in Figure 1), the TOF ratio showed a strong correlation with RE, SE, and RE – SE (the difference between RE and SE) ($r = 0.880$, $P < 0.001$; $r = 0.839$, $P < 0.001$; $r = 0.680$, $P = 0.001$, respectively; Figure 2a). Additionally, in the period between the first rocuronium administration and 80 minutes after increasing the remifentanil dose (180–355 minutes in Figure 1), the TOF ratio also showed significant but relatively low correlation with RE, SE, and RE – SE (the difference between RE and SE) ($r = 0.693$, $P < 0.001$; $r = 0.708$, $P < 0.001$; $r = 0.418$, $P = 0.011$, respectively; Figure 2b). These results suggested that falsely elevated entropy values by EMG contamination could occur without sufficient analgesia.

Discussion

Previous studies demonstrated that the EMG activity could increase easily in the anesthetic situation with no or shallow neuromuscular blockade or with noxious stimuli or insufficient intraoperative analgesia, especially during a light level of total

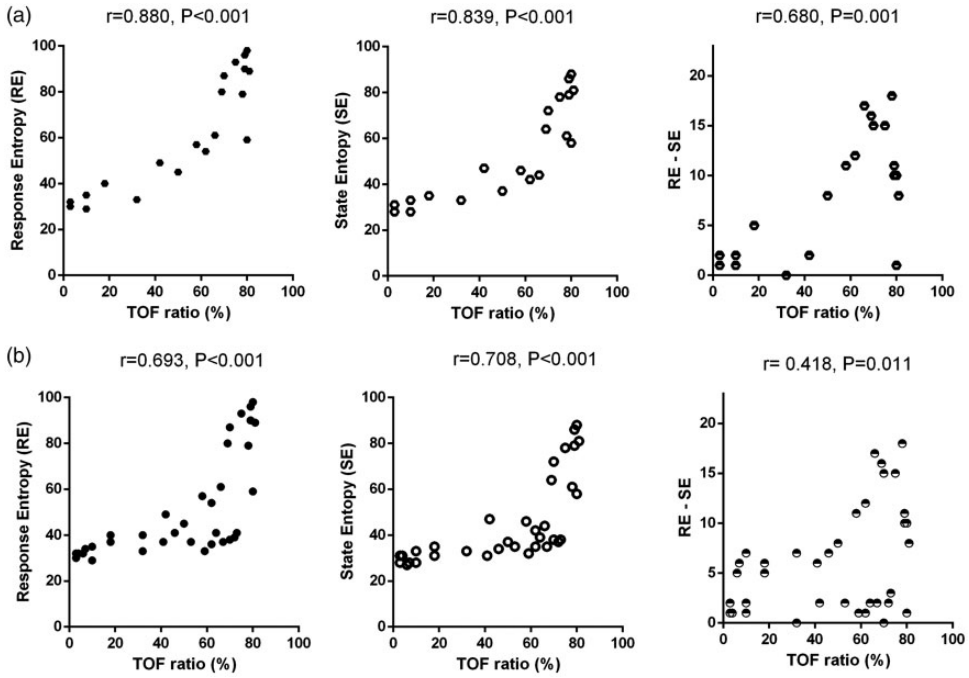

Figure 2. Correlation analysis between entropy indices and the train-of-four (TOF) ratio. Values are the Pearson's coefficients of correlation. SE, state entropy; RE, response entropy, RE – SE, the difference between RE and SE. (a) The time period from the first rocuronium administration to the remifentanil dose increase (180–275 minutes, from the first red arrow to the blue arrow in Figure 1). (b) The period from the first rocuronium administration to 80 minutes after increasing remifentanil dose (180–355 minutes in Figure 1).

intravenous anesthesia, resulting in falsely increased entropy values.[1,2]

Muscle relaxants can suppress EMG activity by decreasing muscle tone and preventing muscle movement. Even in awake persons, neuromuscular block decreased the BIS values.[7,8] Kim et al.[5] reported that BIS, RE, and SE values were all decreased and became similar after injection of the muscle relaxant in patients with myoclonus during induction of anesthesia with etomidate. Additionally, neuromuscular block reversal by pyridostigmine significantly increased RE values in a prospective study.[9] Therefore, no or shallow neuromuscular blockade is most likely to increase the EMG activity, which can inappropriately increase entropy. Recently, Kim et al.[10] added support to this contention with a case of an unusual increase in entropy by EMG activity, which was not indicated by the patient state index.

Nociceptive stimuli are likely to lead to increased RE followed by increased SE in patients who are not receiving neuromuscular blockers.[1] Similarly, noxious pain caused by tracheal intubation can increase EMG activity,[11] resulting in increased entropy values, especially RE rather than BIS.[12,13]

These nociceptive stimuli or noxious pain during anesthesia or surgery will be enhanced in clinical situations that have an insufficient analgesic level.[3]

To date, the false elevation of entropy values resulting from high EMG activity has been reported in patients who underwent total intravenous anesthesia,[1,3,6]

while there is only one report of this occurrence in general anesthesia using inhalational anesthetics.[10] This trend may occur because volatile anesthetics enhance the neuromuscular blocking effects of nondepolarizing muscle relaxants.[14] Aho et al.[6] reported that an increase in BIS and entropy values after sugammadex or neostigmine administration was an electromyographic rather than an electroencephalographic phenomenon, and they concluded that EMG contamination of the EEG caused BIS and entropy values to increase during rocuronium-induced neuromuscular blockade reversal under light propofol-remifentanil anesthesia. In the present case, the same phenomenon of the EMG contamination on the EEG was observed to increase entropy values despite being under desflurane anesthesia.

The raw EEG may provide more detailed and precise information than the entropy value, which is processed data; therefore, we also checked the raw EEG signal during the SE/RE elevation. During the first SE/RE elevation, EEG with low-amplitude and high-frequency oscillations that resembled an awake EEG was observed on the EEG display, and after administering rocuronium and increasing the remifentanil dose, the EEG changed to high-amplitude and low-frequency oscillations. Thus, we judged that the EEG at the elevated SE/RE might be a false EEG that resulted from EMG contamination, while the slow EEG that was shown after administering rocuronium and increasing the remifentanil dose was the true EEG that did not contain EMG contamination.

In certain situations, EEG-based depth-of-anesthesia monitors do not properly detect burst suppression. In a previous report,[15] suppression episodes that were incorrectly detected led to high SE/RE values because of the Entropy module algorithm, which was presumably set to recognize a burst suppression below the threshold value of about 22 μV when the non-linear energy operator was calculated. Muhlhofer et al.[16] described that the patient state index underestimates the occurrence of burst suppression. If the suppression phases contain, for example, electrocardiogram artifacts or an EEG with weak (slow) oscillations (which resemble an awake EEG), these episodes cannot be detected and high index values with a burst suppression ratio of 0 can be the consequence. A desflurane concentration of 7% to 8% in our patient could yield a burst suppression, because a minimum alveolar concentration (MAC) of 1 to 1.2 for desflurane may be sufficient to induce burst suppression.[17] The decrease to the range of 30 to 40 in SE/RE values can occur when burst suppression is present.[15,18] Thus, there was the potential for falsely elevated entropy values with incorrectly detected suppression in our patient.

In conclusion, entropy values can be inappropriately elevated by increased EMG activity, which is caused by a shallow neuromuscular block and insufficient analgesia even during desflurane anesthesia. Therefore, to prevent the increase in entropy values caused by increased EMG activity, we suggest that an adequate degree of neuromuscular blockade, analgesia, and anesthesia should be provided during desflurane anesthesia as well as total intravenous anesthesia. This case shows the limitation of Entropy™ module monitoring. Rather than reading only the entropy numerical value, interpretation of raw EEG and consideration of possible factors that could cause an incorrect entropy value must be kept in mind.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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