Restrict relaxants, be aware, and know the limitations of your depth of anaesthesia monitor

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In this issue of the British Journal of Anaesthesia, Schuller and colleagues examined the effect of neuromuscular block on the EEG bispectral index (BIS) in awake subjects. The researchers induced the scenario of awake paralysis in consenting volunteers.1 Recent data suggest that awake paralysis is one of the main factors for distress during awareness, and may be even more critical than experience of pain.2 Patients with distress during awareness are at high risk to develop long term sequelae. This is consistent with a main mechanism for the development of post-traumatic stress disorder (PTSD), the combination of a traumatizing event and the inability to follow the flight reflex and withdraw oneself from the traumatizing situation.

As a consequence, detection of consciousness seems most important when neuromuscular blocking drugs are administered. As standard anaesthesia monitoring may not detect awareness or consciousness with paralysis, this seems a main target for specific monitoring of the effects of anaesthesia on the main target organ – the brain.

In the last decades, several monitors of the hypnotic effects of anaesthesia have been developed. These measure the EEG and calculate an (alpha) numerical index value reflecting ‘depth’ of anaesthesia or the hypnotic component of anaesthesia. The EEG itself measures electrical activity on the surface of the scalp. It is mainly composed from signals of the brain cortex and muscle activity (EMG). It seems plausible that EEG-based monitoring reflects activity of the main target organ of anaesthesia, the brain.

Currently, development and calculation of indices of the hypnotic component of anaesthesia are based on a probabilistic approach: various parameters, which describe characteristics of the EEG signals, are calculated from the EEG. For an anaesthesia index, these parameters are combined using different proprietary algorithms. For the development of such an index, EEGs are recorded during volunteer and patient studies. Simultaneously, the hypnotic component or the level of anaesthesia is clinically assessed. Calculated EEG data and the results of clinical assessment are stored in a database. Using statistical and mathematical (probabilistic) methods, parameters calculated from the EEG are combined to produce an index value, which corresponds to the observed level of anaesthesia.

This database-driven approach may have limitations, in particular for the detection of intraoperative wakefulness: it is very unlikely that data from an awake and paralyzed subject are included in this database. Therefore, the resulting anaesthesia index has not been trained with a dataset that contains this clinical situation, and it remains unclear whether such a situation is adequately classified by such an index.

Current EEG-based monitors analyse the EEG spectrum in a range where cortex activity and EMG activity overlap.3 As current indices of anaesthesia are calculated with proprietary algorithms, it is unclear to which extent the index is based on analysis of brain activity and to which extent EMG parameters may contribute to an anaesthesia index (i.e. whether a proprietary index may subsequently be influenced by neuromuscular block).

It has been clarified that an index of anaesthesia can be calculated on the basis of spontaneous (EEG) or evoked (evoked potential, EP) electrical brain activity and muscle activity (EMG).4 Even if the EMG is a surrogate measure and does not reflect activity of the main target organ of anaesthesia, the brain, it may still contain useful information. Discomfort may lead to facial muscle activity (grimacing), therefore inclusion of muscle activity into a monitor may increase the sensitivity to detect insufficient blockade of reactions to stimuli. The disadvantage of the inclusion of muscle activity is the potential dependence of an index on muscle activity to calculate an index value that indicates consciousness: neuromuscular block decreases EMG activity and this decrease may lead to a misinterpretation of neuromuscular block as (deep) anaesthesia. This pharmacologically induced decrease of muscle activity (EMG) is not related to sedative or hypnotic anaesthetic effects. Therefore, analysis of the EMG may not be a useful basis for an index of the level of anaesthesia, because neuromuscular block decreases EMG activity and this decrease may lead to a misinterpretation of neuromuscular block as (deep) anaesthesia.

For a previous version of the BIS monitor (BIS A-1000 monitor, BIS version 3.31), a small study in volunteers showed the influence of neuromuscular blocking agents on the BIS index value: with isolated forearm technique, neuromuscular block was induced in awake volunteers, and BIS decreased after administration of succinylcholine, while subjects were able to move the isolated hand to command.4 This study has often been cited, and subsequently the A-2000 monitor and BIS XP™ platform were released. This version of the BIS included a new sensor with an additional electrode above the eyebrow. This additional electrode was designed to identify signals related to muscle activity and the monitor now provides an indicator of EMG activity.

Accordingly, the manufacturer suggested that the new hardware and software had solved the problem, but in daily clinical practice, attention had been directed towards the interference of EMG and EEG signals.5 Dahaba and colleagues tried to analyse the influence of different degrees of mivacurium-induced neuromuscular block on BIS XP™ in patients.6 They found little influence of mivacurium when administered during propofol anaesthesia, with BIS-values between 40 and 50. This confirmed results of a volunteer study with propofol and mivacurium,7 which did also not identify a decrease of BIS values when mivacurium was administered at baseline.
BIS between 40 and 50. Both studies have in common that they analyse the influence of neuromuscular block on BIS values, which are already low after propofol administration. After propofol-induced loss of consciousness, both high frequency components of the EEG and (high frequency) EMG activity decrease. In this situation, additional neuromuscular block may not add much changes to the EEG.

Only if EMG activity is present, administration of neuromuscular blocking agents may change the index value. These changes have been observed in patients during anaesthesia and in the intensive care unit.

The clinical interpretation of this EMG influence requires caution. In many instances, the effect of EMG on BIS was treated as artifact, and the application of neuromuscular blocking agents has been used to reduce the influence of this artifact. Higher index values measured without neuromuscular blocking agent were even judged to be ‘spurious’, and it has been suggested that BIS calculation from a signal containing EMG may lead to an ‘overestimate’ of index values. As the present study of Schuller and colleagues suggests, the values recorded under neuromuscular block may be spurious (i.e. the application of neuromuscular blocking agents may prevent the BIS monitor detecting awareness).

The described misreading of EMG influence arises - at least in part - from the fact that the BIS algorithm is proprietary and unknown to the clinical user: it can only be observed that EMG has an influence on BIS, but it cannot be deducted from the algorithm how much EMG contributes to BIS in general, or how much EMG contributes to calculation of low and high BIS values. The results of Schuller’s study show that the influence of EMG on BIS is so high that the absence of EMG leads to BIS values representing ‘surgical anaesthesia’.

As a consequence of Schuller’s findings, several recommendations and guidelines should carefully be revised: BIS monitoring has been recommended in ICU-patients, in particular when neuromuscular blocking agents are administered. As the present data show, this may in particular be a situation with misleading BIS values.

Despite of these limitations, EEG-based monitoring of the hypnotic component of anaesthesia, has introduced a monitor of the anaesthetic effect on the main target organ of general anaesthesia, into daily clinical practice. With the broader application of monitors of the hypnotic component of anaesthesia, EEG-based monitoring has evolved from a research method to a clinical tool.

It has been demonstrated that after a brief structured training in EEG reading and practical application in the operating theatre, anaesthetists are able to estimate the BIS value from the unprocessed EEG. This demonstrates the feasibility of intraoperative EEG monitoring as an integral part of anaesthesia monitoring. EEG-based monitoring allows a specific assessment of anaesthetic effects on the main target organ of anaesthesia. With the knowledge of its limitations, even the application of an anaesthesia index may be useful. If such an index is used, it is essential to know not only its advantages, but also its limitations, to avoid misinterpretation of index values: as shown by Schuller and colleagues, neuromuscular block may mimic deep anaesthesia index values, even in awake subjects. Thus, the risk of awake paralysis is increased with possible critical consequences for the patient. Therefore, it may be useful to use an EEG-based monitor, but its usefulness under neuromuscular block is limited. This limitation is because of the use of high frequency components of the EEG and the probabilistic approach. By now, our knowledge about mechanisms behind anaesthesia-induced unconsciousness has increased and future research should focus on the development of an index, which is based on underlying mechanisms of anaesthesia-induced unconsciousness. As long as such an indicator is not available, it may be useful ‘to relax, be aware, and know what you are doing’, but more appropriate to restrict neuromuscular block, be aware, and know the limitations of your anaesthesia hypnosis monitor.

Declaration of interest

None declared.

References