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EDITORIAL

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Monitoring sedation in the intensive care unit: can "black boxes" help us?

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Sedation is one of the commonest intensive care treatments. As with any treatment, it has potential side effects [1, 2]. Excessive sedation is prevalent in ICUs, because organ failures result in unpredictable pharmacokinetics and severe illness may alter the pharmacodynamics of drug responses. The delayed recovery of consciousness can prolong mechanical ventilation, increase complication rates and lengthen ICU stay. It potentially affects both the outcome and costs of critical illness [3]. There is a wide variation in sedation practices between intensive care units [4]; finding ways to increase the use of evidence-based approaches should improve the quality of intensive care [5].

One method of reducing excessive sedation is to discontinue sedative drugs completely on a daily basis [6]. This approach may be suitable for many patients, but it is unclear if it has side effects, such as myocardial ischaemia, or if the prevalence of long-term complications, such as post-traumatic stress disorder, is increased [7, 8]. Daily awakening also demands considerable nursing experience and may be perceived as insensitive to individual patient needs. It would certainly be useful to have methods of "fine-tuning" this approach.

At present monitoring sedation relies on clinical judgement and the use of various sedation scores. Even when included in protocols, sedation scores are influenced by subjective judgements [9]. Some, such as the Ramsay score, were not developed for use in ICUs and have never been properly validated [1]. Others, such as the Sedation-Agitation Scale, were developed specifically for ICUs, but remain subject to problems with consistency and inter-rater variability [1, 10]. These scales are particularly insensitive to change at deeper levels of sedation, which is exactly when a sensitive measure is needed to avoid excessive sedation. It would be useful to have a monitor that could detect changing levels of consciousness when clinical signs become unreliable.

The apparently obvious solution is to assess brain function directly using electroencephalograph (EEG) analysis. However, the EEG is a complex signal and the interpretation of signals requires complex mathematical approaches to generate summary "magic numbers", which are supposed to correlate with particular clinical states. As a result, unless used by enthusiasts with an interest in the area, these systems are usually viewed as "black boxes". Clinicians therefore have to trust that the monitors do the job that they claim to do.

Recently two new systems based on EEG analysis have been introduced to monitor the depth of anaesthesia in the operating theatre. These are the BIS (Aspect Medical Systems, Natick, MA) and Spectral Entropy (Datex-Ohmeda, Helsinki, Finland). These systems were developed primarily to avoid awareness, with potential secondary benefits including lower drug costs and quicker recovery. Both use raw EEG and electromyogram (EMG) signals collected via forehead electrodes. They differ in the way the signals are processed mathematically. BIS uses three sub-parameters (burst suppression; the beta ratio and SynchFastSlow) and a weighting algorithm that has not been made widely available for scrutiny [11]. The Entropy system analyses the whole spectrum of physiologically relevant frequencies and has been published [12]. It is tempting to take these black boxes to the ICU and try to use them as sedation monitors. For BIS this has already been done, with mixed results [13, 14, 15, 16].

However, if we set aside the potential of using the newest black box to generate a publication, what are the problems that need to be addressed systematically in the ICU environments?

Signal acquisition

Acquisition of the EEG and facial EMG (fEMG) signals in the ICU presents challenges that are less problematic in the operating theatre. The sensors need to be positioned correctly and remain adherent for long periods in patients who may be moving themselves or may be moved passively for pressure care or physiotherapy [17]. Disconnection should be obvious to nursing staff, but more subtle changes in adherence could alter the conductance of the skin-electrode contact. Although systems created for anaesthesia have in-built alert systems to examine electrode contact, these have not been validated in the intensive care environment. In addition, whereas optimum anaesthesia is characterised by dry skin, critical illness is associated with sweating. It is presently unclear if these factors are sufficiently accounted for in BIS and Spectral Entropy or how well the systems cope with the changes in conductance that accompany sweating. It is also not known if long-term placement on patients' foreheads, a very visible part of the body, has any adverse skin effects. This may appear trivial to medical staff, but could be important to relatives and patients.

Although there are increasing numbers of machines in operating theatres, these are few compared to those involved in the care of many patients in the ICU. All of these emit frequencies that, in theory, could combine with the EEG signals obtained from the patient and result in artefacts. Electric beds, haemofiltration machines, ventilators and infusion pumps are examples, but even the vibration of secretions in ventilator tubing has the potential to be problematic [18]. BIS and Entropy focus on frequencies in the 0–47 Hz range and it is currently unclear whether the existing artefact suppression algorithms are adequate. It is certainly presumptive that those developed for the operating room are good enough for the ICU.

Signal processing

There are several reasons why the correlation between the processed EEG signals obtained during critical illness and conscious level may be different from those obtained in patients undergoing anaesthesia. These include fEMG activity, encephalopathy and temperature variation.

Facial electromyogram activity

Facial EMG signals are a problem when trying to interpret the EEG. fEMG activity is thought to occur mainly in the frequencies over 20 Hz ranging up to 500 Hz; this clearly overlaps with the spectrum of EEG frequencies [19]. The challenge with EEG analysis is to identify clearly the confounding effect of EMG, so that it can be adjusted for. One approach is to exclude this signal from the data used to derive a measure of awareness. The danger with this approach is that important EEG information may be excluded, reducing the value of the derived "magic number". If the exclusion algorithm leaves some fEMG activity in the processed data, the algorithm may interpret these signals as an increase in conscious level. Although fEMG activity is higher when patients are more conscious, it is a non-specific measure, altered by nociceptive stimuli and other factors as well as consciousness. Newer versions of BIS try to identify when fEMG activity is increased and the entropy algorithm presents two "magic numbers", the state entropy (based on the entropy of frequencies 0–32 Hz) and response entropy (based on the entropy of signals 0–47 Hz) [12]. A larger value for response entropy compared to state entropy is intended to indicate when fEMG is active.

For anaesthesia, knowing when there is fEMG is potentially useful, because it may indicate light anaesthesia or imminent emergence during recovery. Is this the case in the ICU? Resorting to muscle paralysis or very high sedative drug dosing is considered sub-optimal practice by most intensivists. Optimal sedation is often defined as an easily rousable or responsive patient, which means that fEMG will be present much of the time or occur intermittently in response to stimulation. Some of the stimulations critically ill patients receive are intense, such as tracheal suctioning or physiotherapy, so the presence of fEMG is unlikely to exclude over-sedation reliably. It is naive to think that black boxes designed to monitor anaesthesia, during which fEMG usually triggers an increase in drug dosage, will work equally well in the ICU, where a conscious level associated with intermittent or continuous fEMG is considered desirable.

Encephalopathy

The vast majority of patients presenting for anaesthesia have a functionally normal brain. This is not so in the ICU. Recent studies in non-sedated critically ill patients suggest that up to 70% have clinical evidence of altered consciousness consistent with an encephalopathy [20, 21, 22, 23]. The precise prevalence of critical illness encephalopathy is not known; this is partly because there is no agreed way of diagnosing it and because the use of sedative drugs makes it difficult to detect. The EEG findings in encephalopathy have many similarities to those during sedation and anaesthesia [24], which is potentially a major problem for a black box designed for patients with normal brains. At present we do not know if the effects of ICU encephalopathy and sedative drugs on the brain and the EEG are additive, synergistic or have some other relationship. Both Spectral Entropy and Bispectral Index are indicators of cortical activity, rather than consciousness *per se*. It is not clear how they perform when cortical activity is altered by metabolic and disease processes as well as sedation [25].

Temperature

Patients in the ICU are frequently pyrexial or hypothermic either as a consequence of their illness or in response to therapies. Temperature is known to affect the EEG signal and has already been identified as a factor that can alter BIS values [14]. At present the interaction between temperature, sedation level and EEG are not understood.

The goal of producing a monitor that tells us about our patients' sedation level is timely, and a monitor that works would significantly improve the care of sedated critically ill patients. We have highlighted some of the key issues that we need to address during research and development of these tools. There is no doubt that the recently produced "black boxes" will be evaluated as sedation monitors in the ICU. However, we should not be surprised if the tools do not work in their current form. Rather than accept the black boxes given to us, we should open them and work with those who understand them to answer our own questions.

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