Memory and awareness during anaesthesia

Memory and Awareness 7, MAA7, is the latest in a distinguished series of triennial conferences which were started in 1989 by Dr Benno Bonke, Prof Keith Millar, and Dr Bill Fitch. Bringing together clinicians, basic scientists, engineers, psychologists, and patients, it offers a unique forum to explore all aspects of perioperative awareness and depth of anaesthesia (DOA) monitoring. By chance, the meeting coincided with the publication of the B-Unaware study1—of which more later.

Where are we with DOA in early 2008? A good place to start is understanding how sedative–hypnotic drugs affect memories as they are progressively transferred from initial registration through short-term memory to long-term recall.2 Veselis and colleagues2 studied event-related potentials (ERPs) which are correlates of memory processing. Subanaesthetic doses of drug did not affect performance on the encoding task but did impair ERPs and long-term retention of memory. The amnesic effects of propofol and midazolam seem to begin between 6 and 27 s after stimulus registration, suggesting that they have some impact on memory function soon after registration.

Unpicking the mechanism of anaesthesia remains an important objective. Although the molecular interactions between anaesthetic agents and the GABA_A receptor are now reasonably clear,3 the effects these produce at a tissue level are harder to understand. Investigation of anaesthetic effects on brain slices4 5 illustrates the ability of anaesthetics to induce state changes in neuronal circuits. At a whole organism level, studies of chronically instrumented rats suggest that the transition to unconsciousness involves disruption of cortical function6 with subsequent descending influences on the thalamus where nicotinic receptors may control the switch between the conscious and unconscious states.7 In humans, functional MRI and PET imaging studies have clarified the site and sequence of anaesthetic actions on the cortex8 and such investigations appear to give a consistent story to that derived from animal work.

So much for mechanisms, how about awareness? Despite increased attention from clinicians, patients, and the media, awareness continues to occur in both adults (0.13%)9 and at a higher rate in children (0.8–1.2%).10 Anaesthetic awareness is a potent precipitant for post-traumatic stress disorder (PTSD) and there is a convergence of psychologists’ thinking on therapy. Although a routine referral for specialist PTSD assessment is recommended for those in whom unambiguous awareness has occurred, PTSD symptoms will spontaneously remit in a significant minority. Trauma-focused cognitive behavioural therapy is best reserved for those whose PTSD symptoms have persisted beyond 1 month.11

Signal processing continues to develop with several new approaches for deriving DOA information by processing the EEG. Although simple single techniques such as permutation entropy12 can produce robust-derived parameters, commercial DOA systems typically use several EEG processing techniques to quantify electromyogram, beta activity, and synchronization. The bispectral index (BIS) remains the most intensively researched system. However, several competitors have achieved equivalent performance as measured by the prediction probability (Pk)13 used to compare DOA technologies.

At the start of this editorial, we referred to the B-Unaware study1. Investigators randomized nearly 2000 patients at high risk for awareness into two groups: BIS monitored (target range 0.7–1.3 MAC, including nitrous oxide). In both groups, the alarms were set to indicate care outside of the target range. Modified Brice interviews14 (the ‘gold standard’ for postoperative awareness screening) were conducted on three occasions: within 24 h after operation, between 24 and 72 h, and again at day 30, replicating the ‘gold standard’ for postoperative awareness screening) were conducted on three occasions: within 24 h after operation, between 24 and 72 h, and again at day 30, replicating the screening protocol of the B-Aware study.15 The investigators found definitive awareness in two patients in each treatment group giving an identical incidence of 0.21%, which was significantly less than the 1% expected in this high-risk population. The authors concluded that ‘our findings do not support routine BIS monitoring as part of standard practice’.

Essential to this conclusion is the assumption that the ETAG group received care that was ‘standard practice’. Although end-tidal gas monitoring is common, it is not universal practice to deliver 0.7–1.3 MAC with alarms enabled to all patients, including those with significant co-morbidities. Indeed, some of the anaesthetists found it difficult to maintain the proscribed levels of agent concentration as there were sustained periods of ETAG levels below 0.7 MAC in 74.5% of patients. In this light, it is more reasonable to consider the ETAG group as cared for by not ‘standard practice’ but by an experimental anaesthetic delivery protocol designed to limit awareness. Further, the B-Unaware MAC calculation included concomitant nitrous-oxide. Although the additivity of MAC fractions of nitrous oxide and inhalation agents for the suppression
of reflex responses is well recognized, their interaction on memory formation is less clear and cannot be assumed to be additive, that is, we cannot be sure that 0.7 MAC isoflurane is equivalent (in this regard) to 0.7 MAC of an isoflurane/nitrous oxide mixture. The investigators have shown that both awareness risk-reduction strategies, BIS monitoring, or care by anaesthetic protocol, work equally well, an important observation.

This observation is corroborated by the study of Pollard and colleagues who utilized a quality assurance database to demonstrate a very low incidence of awareness in their patient population: 0.13% in their high-risk patients and 0.0024% in their low-risk patients. This study has generated controversy about its design, but somewhat lost in the debate is the fact that patients were cared for with anaesthetic delivery protocols. Although the paper does not describe these protocols in detail, they included (i) halogenated anaesthetic gases at 0.5–0.8 MAC, (ii) no nitrous oxide use, (iii) avoidance of short-acting narcotics, and (iv) avoiding a culture of rapid room turnover as the paramount anaesthetic goal (R. J. Pollard, personal communication, March 25, 2008). The low incidence of awareness in high-risk patients in this study, when considered in the context of the recent B-Unaware study, suggests that care by anaesthetic delivery protocols that mandate a particular level of halogenated agent delivery may effectively limit awareness. Implicit in this, however, is being sure that an adequate level of agent is being delivered, emphasizing the importance of having alarms enabled to prevent the undetected dry vaporizer.

Practical considerations suggest that protocol-driven inhalation anaesthesia without DOA monitoring may expose some patients to higher inhalation agent concentrations than they actually require. Is this a bad thing? Although some preliminary reports have suggested that excessive anaesthesia impairs outcome, these should only be considered hypothesis generating and further research is required. Likewise, the clear evidence of anaesthesia-induced neurotoxicity in neonatal rat pups is worrying, but its relevance to humans is unknown. Helpfully, the current GAS study [a multi-site randomized controlled trial comparing bupivacaine (regional) anaesthesia and sevoflurane (general) anaesthesia for effects on neurodevelopmental outcome and apnoea in infants undergoing unilateral or bilateral inguinal hernia repair] which randomizes neonates requiring hernia surgery to general or spinal anaesthesia will directly address this question. However, the need for prolonged neurobehavioural assessment during the follow-up period will require us to wait patiently for the results.

Where does this leave us? It has taken decades for the anaesthesia community to accept that awareness is a reality. Subsequently, cohort studies and the B-Aware study have sought to convince us that the incidence of awareness can be reduced. Uptake of this message has been patchy, and many anaesthetists believe that the evidence is insufficient to justify general application of DOA monitoring. B-Unaware takes us a step further—but in which direction?

Nihilists will use this as ammunition to condemn DOA monitoring and represent B-Unaware as grounds to disregard it. A moment’s reflection suggests a more important double message. First, we can now clearly state that the incidence of awareness can be reduced—and in a population broadly applicable to a good proportion of our general workload. Second, we have a choice. We can decrease awareness by using DOA monitoring or by taking a protocol-driven, structured and fully alarmed approach to our anaesthetics. Finally, we should remember another key message. B-Unaware does not mean business as usual—instead, it makes us choose between two approaches which have been shown to be effective. Since most of us use neither a DOA monitor nor maintain a minimum of 0.7 MAC inhalation anaesthesia with an alarm set, each of these alternatives require us to modify contemporary practice. B-Unaware does not provide an excuse for simply doing nothing. Last year you might have faced a patient demanding a DOA monitor be used for their anaesthetic. This year you might reasonably be asked whether you will be using an inhalation technique with an alarm set at 0.7 MAC. After B-Aware and B-Unaware, we should not B-afraid, but we should certainly B-prepared!

J. R. Sneyd*
D. M. Mathews

1 Peninsula College of Medicine and Dentistry
The John Bull Building
Tamar Science Park
Plymouth PL6 8BU
UK
2 New York, USA

*E-mail: robert.sneyd@pms.ac.uk

References
6 Hudetz AG. Anaesthetic unconsciousness as a result of cortical disintegration. Br J Anaesth 2008; 100: 868P
8 Ramani R, Qiu M, Constable RT. Sevoflurane 0.25 MAC preferentially affects higher order association areas: a functional magnetic
16 Chortkoff BS, II, Bennett HL, Eger EI, II. Does nitrous oxide antagonize isoflurane-induced suppression of learning? Anesthesiology 1993; 79: 724–32
19 Sebel PS, Bowdle TA, Rampil IJ, et al. Don’t ask, don’t tell. Anesthesiology 2007; 107: 672

doi:10.1093/bja/aen128

Editorial IV

Volume 100: Case reports: should they be confined to the dustbin?

A tale should be judicious, clear, succinct;
The language plain, and incidents well linked;
Tell not as new what ev’ry body knows,
And new or old, still hasten to a close.

Conversation, 1782.
William Cowper, English Poet

Since time immemorial, editorial boards have agonized about publishing case reports in their journals. Will they denigrate the standards of their journal and most importantly, will they have a disadvantageous effect on their impact factor? The agony continues as most of us enjoy reading a tale of horror (especially if we do not experience it first hand). It must be acknowledged that case reports attract readers, often clinicians, who may not, alas, look at other parts of the British Journal of Anaesthesia in the same detail. But most importantly, a case report should only be published if it adds to our knowledge or improves our practice. Tales of woe, especially followed by the death of a patient, are insufficient.

Almost all medical journals publish case reports. Historically, they have been an integral component of any clinical journal. However, for the reasons given, there has been a gradual decline in the numbers published in leading medical journals in recent years. For instance, we have estimated that, in the British Journal of Anaesthesia, over the last decade, the number of case reports has decreased by one-third. In contrast, with the ever-increasing numbers of online journals, there is now a journal dedicated only to publishing case reports (www.jmedicalcasereports.com).

Editors of medical journals are under growing pressure only to publish articles that will be cited. Although the number of citations of an article does not necessarily reflect how widely the article has been read, currently the citation index is the most accepted method of assessing the credibility of an article. Thus, if editors are only subservient to external pressures, they would fill their journals with randomized controlled trials and no case reports. In the medical literature, randomized controlled trials, which are considered to be Class 1 scientific evidence, are undoubtedly the most-cited. They are most likely to increase the citation index and hence the impact factor of the journal.1 This is of great importance to any editor as the status of their journal is ranked according to its impact factor. It affects academic promotion in Europe. One may