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Editorial III

Remembering awareness†

This edition of the British Journal of Anaesthesia includes abstracts from the Sixth International Symposium on Memory and Awareness in Anaesthesia, which was held in Hull during June 2004. These symposia have a distinguished pedigree going back to the 1980s when Dr Benno Bonke joined with Professor Keith Millar and Dr William Fitch to plan the First International Symposium on Memory and Awareness.

†This Editorial accompanies the Memory and Awareness Symposium Abstracts. (Br J Anaesth 2004; 93: 482–94P)

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which took place in Glasgow, Scotland in 1989. This and subsequent meetings have channelled and developed critical thinking on consciousness, memory, and information processing in the perioperative period. The 2004 symposium coincided with the publication in the Lancet of an important paper by Myles and colleagues, who, for the first time, demonstrated in a prospective, randomized controlled trial that the use of intraoperative depth of anaesthesia monitoring substantially reduced (by 82%) the instance of awareness in a defined patient population.1

Commercial interest in depth of anaesthesia monitoring is at an all-time high, and this was evidenced by the substantial trade presence at the Hull symposium. Several commercial systems for intraoperative use are now commercially available (Table 1), although only the bispectral index (BIS) monitor makes a specific claim to reduce the incidence of awareness.

What has provoked this upsurge of interest in commercializing depth of anaesthesia measurement? Although reports of intraoperative awareness have circulated for years, both anecdotally and as case reports,1 2 it is only relatively recently that the true incidence of conscious awareness during anaesthesia has been properly documented. In a prospective survey of 11 785 patients who had undergone general anaesthesia in two Swedish hospitals between 1997 and 1998, in at least one of three postoperative interviews, awareness was reported in 0.18% of cases in which neuromuscular blocking drugs were used, and 0.1% in cases where they were not.3 Importantly, this study reported that a single early interview would only have revealed 11 of the 18 cases, and that a series of interviews appears to be necessary to accurately detect such episodes. A similar rate of awareness, 0.11%, was found in a separate study of 10 811 patients anaesthetized in an Australian hospital.5 Preliminary data presented at the Hull meeting suggest that the incidence of awareness in children may be even higher than in adults.6

Does depth of anaesthesia monitoring reduce the instance of awareness? Initially this question was thought refractory to clinical research. A power analysis to estimate how many patients would be needed to demonstrate a reduction of awareness in clinical practice, with a baseline incidence of 1/500, suggested that 5245 patients per group would need to be recruited to have a 90% chance of demonstrating a reduction in the incidence of awareness between monitored and unmonitored patients, and many more if the incidence were smaller.7 Since then, two alternative research approaches have been used to address the sample size issue. First, a prospective cohort of 4945 patients undergoing anaesthesia including the use of muscle relaxants were monitored with BIS, and their incidence of awareness (0.04%) compared with the higher rate (0.18%) determined in an historic control group.8 Recently, the Australian group led by Paul Myles, circumvented the sample size issue by selectively studying patients considered to be at high risk;1 these researchers also used a large estimate of effect in their power calculation, a bold move that was justified by their results.

Where does this leave us? It is now clear that, at least in high-risk patients, use of the BIS does reduce the incidence of conscious awareness with recall during anaesthesia. Furthermore, it is clear that several postoperative interviews are necessary if the full incidence of awareness within any patient group is to be determined, and the sample size calculation for prospectively demonstrating the same effects in standard ‘low-risk’ patients remains daunting. In a previous editorial for this journal, I expressed concern that perioperative use of the BIS monitor might tempt anaesthetists to ‘skate on thin ice’,9 and by reducing their administration of anaesthetic agents, actually increase the risk of awareness in their patients. This concern has not yet been realized, and BIS monitoring has been shown to reduce anaesthetic drug use and to accelerate patient eligibility for discharge.10 11 In addition, evidence is emerging that use of BIS monitoring may improve other outcomes of anaesthesia including postoperative nausea and vomiting.12 At first sight, reports that using depth of anaesthesia monitoring can both reduce awareness, at least in some patients, and drug consumption, seem contradictory. Reduction in the overall amount of hypnotic administered to a group of patients might be expected to increase rather than decrease awareness. That this is not so, suggests that this monitoring allows tailoring of the dose to the individual by the detection of discreet episodes of arousal or, perhaps crucially, periods of technique failure (interrupted drug administration, wrong vaporizer settings, etc.). This hypothesis is at least compatible with a general reduction in drug dosage but will probably be hard to prove.

Should we be using a depth of anaesthesia monitor for every case? Both manufacturers and some patients who have experienced perioperative awareness would wish us to. However, uptake of these technologies is certainly not yet general, suggesting that either anaesthetists, their managers or their budget-holders are not yet convinced. Whether usage does become general will be determined by a combination of marketing, patient pressure, budgetary considerations and, hopefully, good science.

What about the other depth of anaesthesia monitors? Only the BIS has convincing data to support its efficacy in preventing awareness, albeit only in selected patients. However, when BIS and Auditory Evoked Response (AER) were compared in a three-way comparison with an unmonitored control group there were no differences between the two monitors in terms of patient outcomes.13 Perhaps what matters is the use of an anaesthesia depth monitor rather than the particular use

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of BIS? At present, this can only be considered a hypothesis but one which is of course testable. Individual monitors rely on different technologies, such as polyspectral analysis, EEG entropy and AEP, and extrapolation of results between systems that monitor anaesthetic depth by completely different principles may be hard to justify.

Can the Myles study1 be repeated? Even if depth of anaesthesia monitoring is not universal, it may be hard to convince an ethics committee to permit a replicate study using another monitor, given the impressive performance of the BIS monitor. Were two systems to be compared head-to-head, then the resulting equivalence study would require a separate, different power calculation, and inevitably be much larger and, therefore, more expensive and protracted. Other problems also exist for equivalence studies, and it is not clear that the regulatory authorities would accept such data. Has the Myles study closed the door on other systems? This can only be determined by the regulatory authorities, ethical committees and finally by the willingness, or otherwise, of competing manufacturers to fund the necessary trials. Certainly, the BIS currently has a big lead in terms of quality and quantity of research studies, and it is far from clear whether its competitors can catch up.

What else might depth of anaesthesia monitoring be used for? Is mortality increased in patients with low intraoperative BIS? A prospective study comparing two groups of patients anaesthetized with either a ‘low’ BIS scheme or a ‘high’ BIS scheme of anaesthesia in which both groups were anaesthetized sufficiently deeply to minimize awareness, could answer this question, although patient numbers would probably be large. Patient satisfaction and other outcome data also await exploration in well-designed studies. Finally, the same or similar technology may be applicable to degenerative brain diseases, including Creutzfeldt-Jakob Disease and Alzheimer’s and preliminary research in these areas is already underway.

In conclusion, memory and awareness remains a lively and important area of research and technological development. Clinicians can expect new equipment, supported by a range of clinical research. How they choose to interpret the research and use the equipment will, as ever, remain subject to their personal clinical judgements.

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Declaration of interest
Professor Sneyd is an advisory board member for Organon Inc. Aspect have provided Professor Sneyd with free EEG electrodes for a project unrelated to depth of anaesthesia monitoring.

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