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Awareness and memory function during paediatric anaesthesia

J. Andrade[1]*, C. Deeprose[2] and I. Barker[3]

[1]School of Psychology, University of Plymouth, Drake Circus, Plymouth PL4 8AA, UK. [2]Department of Psychiatry, University of Oxford, Oxford, UK. [3]Department of Anaesthesia, Sheffield Children's Hospital, Sheffield, UK

**Corresponding author. E-mail: j.andrade@plymouth.ac.uk*

Background. Previous research indicates a much higher incidence of awareness during anaesthesia in children than in adults. The present study is the first large-scale, intraoperative assessment of awareness during paediatric anaesthesia using the isolated forearm technique, and the first large-scale study of memory function during paediatric anaesthesia.

Methods. One hundred and eighty-four children, 5–18 yr, underwent the isolated forearm technique during the first 17 min of surgery while receiving volatile anaesthesia. The isolated forearm technique was modified to accommodate brief or no paralysis. Bispectral index was monitored in a subset of 54 patients. Sixteen neutral words were played 20 times during surgery and, on recovery, implicit memory for these words was tested with a word identification task. Explicit memory for the surgical period was tested with a structured interview. Behavioural changes were assessed with age-appropriate questionnaires.

Results. No child had explicit recall of intraoperative events on recovery, and there was no evidence of implicit memory for words presented during anaesthesia. Two of 184 children made unambiguous and verified responses on the modified isolated forearm technique, an incidence of intraoperative awareness of 1.1%. One of these children reported that he was uncomfortable and not completely unconscious during surgery. Neither child had implicit memory for the neutral words, or adverse behaviour change.

Conclusions. The incidence of awareness during surgery in children is approximately eight times that measured in adults by postoperative recall. In contrast to adults, there is no evidence for preserved memory priming during anaesthesia.

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Recent research with children indicates an incidence of awareness during anaesthesia between 0.8%[1] and 1.2%,[2] at least six times higher than the incidence of 0.13% observed in adult patients.[3] Adults who recall waking up during their operation have been observed to suffer from psychological problems, including insomnia, general anxiety, nightmares, and intrusive memories or flashbacks.[4 5] The figures quoted are likely to underestimate awareness because they are based on patients' postoperative recall. Patients are prone to normal forgetting and anaesthetic drugs have specific amnesic effects.

Research using the isolated forearm technique[6] shows that the true incidence of intraoperative awareness is at least four times the incidence suggested by postoperative recall.[7] The isolated forearm technique involves inflating a cuff around the patient's forearm just before injection of neuromuscular blockers, leaving the forearm free to move even though the rest of the body is paralysed for surgery. Awareness is indicated by motor responses to commands to move the isolated hand.

Most studies using the isolated forearm technique have been small-scale, and this is true of the only published study of the technique with children. Byers and Muir[8] tested 41 children about to undergo adenoidectomy with thiopentone induction and halothane–nitrous oxide maintenance of anaesthesia. Eight of these children (19.5%) reported positively to isolated forearm commands during or after tracheal intubation. None subsequently recalled intraoperative events. The aims of the present study were primarily to extend Byers and Muir's findings by measuring awareness in a much larger sample assessed during rather than before surgery, and second to test the effects of intraoperative awareness on children's memory and behaviour on recovery.

In adults, there is evidence of continued memory function even during deep anaesthesia.[9] Presenting words during surgery activates or 'primes' mental representations of those words and thus facilitates a response to, or with, those words on recovery even though patients have no conscious or explicit recollection of the words.[10] This facilitated responding as a consequence of prior exposure is known as implicit memory. The effects of this preserved implicit memory on patients' subsequent well-being are not known but it is conceivable that priming of existing anxieties, for example, by negative operating room comments, may contribute to symptoms of trauma on recovery.[11 12] Implicit memory develops early in childhood, reaching adult levels from as early as 3 yr of age,[13] so children are hypothetically also at risk of memory priming during surgery. Previous studies of intraoperative memory priming in children reported null results but were small-scale and used relatively insensitive memory tests.[14–16] The present study used a carefully validated test of memory priming during surgery in a large sample of children to achieve a third aim of detecting priming during deep anaesthesia.

Methods

The study was approved by the South Sheffield Medical Ethics Committee and took place at the Sheffield Children's Hospital, Sheffield, UK. Only patients who were ASA I or II, aged between 5 and 18 yr, and who spoke English as their first language were considered. Patients with known visual or hearing impairments, language difficulties, neurological disorders, or who were taking medication known to affect the central nervous system were excluded. Patients having surgery that precluded the use of headphones were also excluded.

To minimize age differences in memory test performance due to vocabulary knowledge or spelling ability, we used a word identification test to measure implicit memory. For this test, participants listen to words embedded in white noise and repeat aloud any words they manage to identify. Implicit memory is indicated when prior presentation of words leads to greater correct detection of those target words than distractor words. All words on the test were common vocabulary items for 4-yr-old children.[17]

A pilot study assessed the sensitivity and purity of the word identification test. A total of 32 children [mean (range) age 6 (4–14) yr] attending Sheffield Children's Hospital Outpatient department listened to a single presentation of one of two lists containing 20 words spoken clearly against a quiet background at a rate of one word per second. Half the participants were asked to listen carefully to these words (full attention condition). The other half heard the words while carrying out a paper-and-pencil visual search task that required them to look for target pictures, shown on the left-hand side of the paper, in arrays of pictures on the right-hand side (divided attention condition). The purpose of this task was to minimize deliberate learning strategies that would be absent during anaesthesia. Participants then attempted the word identification test and a yes/no recognition test. For the recognition test, participants heard 10 of the previously presented target words and 10 distractor words, presented clearly and singly in random order. Participants were asked to say 'yes' if they remembered hearing the word in the first phase of the experiment, and 'no' if they did not. For the word identification test, the other 10 target words and 10 distractor words were played in random order embedded in white noise using SoundEdit software. Each test item was presented once and followed by a pause until the participant responded. Participants had to respond with the exact target word for their response to be scored as a hit, so, for example, 'dinners' would be scored as an incorrect response to 'dinner'. Use of the two 20-word lists as targets or distractors, assignment of words to recognition or word identification tests, and order of the recognition and word identification tests were all counterbalanced. Presentation was controlled by PsyScope software[18] on an Apple Macintosh G4 Powerbook.

For the word identification test, the pilot study showed a memory priming effect size of 0.80 for the difference between target and distractor detection rates in the divided attention condition where children were concentrating on the visual task during word presentation. A mean of 6.13 target words were detected compared with 4.94 distractor words (P=0.002, one-tailed t-test). A memory priming score was calculated for each participant by subtracting the number of distractor words detected from the number of target words detected. The mean of these memory priming scores was 1.19, or 0.07 expressed as a proportion for comparison with previous studies. Children in the pilot study had some explicit memory for the target words, measured using the yes/no recognition test. Explicit memory is sensitive to manipulations of attention, so to check that this explicit memory did not contaminate performance on the putative implicit memory test, we compared word identification performance in the full and divided attention conditions. If the word identification test provides a relatively pure measure of implicit memory, performance on it should be unaffected by manipulating attention. This was indeed the case: performance was similar under full and divided attention conditions at study (P=0.18).

The yes/no recognition test was dropped for the main study to maximize the chance of observing any implicit memory function during anaesthesia; performing two memory tests may have compromised the sensitivity of either test. Items that were routinely too easy or too hard to identify on the word identification test were removed, giving two lists of 16 words each (Appendix A). Use of these two lists as targets or distractors was counterbalanced across patients, so that a random half of the children had a particular word as a target word whereas the same word was a distractor for other children. For each participant in the main study, the target list was presented a total of 20 times during anaesthesia. As in the pilot study, the target items were spoken clearly against a quiet background at a rate of one word per second.

The word identification test comprised four practice words followed by a series of 16 previously presented target words and 16 distractor words embedded in white noise and presented in a different random order for each patient. Each test item was presented once and followed by a pause until the participant responded.

Anaesthetists were informed of the study, and asked to give their typical anaesthetic for each patient based on their preoperative assessment, although they were assured they would be informed immediately if the patient responded to command during the study period. Anaesthetic techniques consisted of propofol with or without an opiate, or sevoflurane, for induction, and isoflurane or occasionally sevoflurane, plus nitrous oxide and oxygen for maintenance. Non-paralysed patients underwent normal induction. For paralysed patients, induction proceeded as normal but before administration of neuromuscular blocking agent, an arterial pressure cuff was applied to the forearm of the non-cannulated arm, over a cotton wool pad, and inflated to 50–90 mm Hg above systolic pressure. This served to isolate the forearm from the paralysing effects of the neuromuscular blocking agent. To allow checks on the integrity of the isolated forearm and on the status of neuromuscular block, electrodes were applied to the skin over the ulnar nerve of each arm, so that a peripheral nerve stimulator could be connected. In a subgroup of patients (n=54), bispectral index (BIS) was used as additional measure of depth of anaesthesia. In these cases, a BIS Pediatric Sensor (Aspect Medical Systems, Newton, MA, USA) was attached to the patient's forehead after induction of anaesthesia and before surgery. The sensor was connected to an A-2000 BIS XP monitor system (Aspect Medical Systems). This monitor was only available in the latter part of the study. It was used in all those patients for whom operating procedures allowed time for setting up.

Experimental stimuli were presented using a portable compact disc player (Sony D-EJ758CK). In the operating theatre, the headphones from the player were placed in the patient's ears and secured with surgical tape. Unique recordings were prepared for each patient, which included the patient's name and a different random order of the stimulus words for each patient. The study period, which lasted for 17 min, commenced at surgical incision with playing of the first command to move: '[patient's name spoken twice], this is Dr Deeprose speaking. Please squeeze your right/left hand. Please squeeze your right/left hand'. These commands were played to every patient, including those who were not paralysed. We use the term modified isolated forearm technique (mIFT) to refer to the general procedure of giving commands to move and observing responses from a non-paralysed hand, where the hand is either isolated from neuromuscular block or where neuromuscular block is not used. For simplicity, we use the term 'isolated forearm' to refer to the monitored arm regardless of whether the arm had to be isolated from neuromuscular block. When a patient responded to command, the experimenter paused the disc and repeated the command. If a patient responded to this repeated command, the initial response was deemed 'verified', otherwise it was recorded as 'ambiguous'. After a verified command, the patient was given two follow-up commands: 'If you are in pain, please squeeze your right/left hand twice' and then 'If you are comfortable, please squeeze you right/left hand twice'.

The first command to move was followed by five repetitions of a randomly assigned 16-word list. This sequence of command plus word list was completed a further three times, and finished with the fifth and final command to move. The integrity of the isolated forearm was checked immediately before each command to move using a train of four twitches, and visually inspected by the experimenter (C.D.) for movement in response to command. The majority of 'paralysed' patients received neuromuscular blockers for intubation only. The cuff was deflated as soon as arm movement was regained in the un-isolated arm, as indicated by a train of four twitches, and the study phase continued as for unparalysed patients. The experimenter recorded clinical and anaesthetic variables immediately after each mIFT command. BIS data were recorded continuously from the first to last command to move and stored on an IBM ThinkPad laptop. Anaesthetists remained blinded to BIS at all times.

On the day of the operation (day 1), consent for participation in the study was obtained and a general medical history relating to previous healthcare experiences.[19] Parents of children aged <13 yr completed a behavioural questionnaire, as used by Kotiniemi and colleagues.[19] The first part of this questionnaire assessed the frequency of behaviours such as crying and attention-seeking on a scale of: 1, never; 2, occasionally; and 3, frequently. On days 2 and 7, parents completed a second version of this questionnaire, which asked about the frequency of the same behaviours relative to before the operation (1, less; 2, same; and 3, more than before). Children aged 13 or older completed a shorter and more age-appropriate version at the same intervals, using the same scales to rate how often they felt tearful, anxious/worried, had problems sleeping, felt happy, felt at ease. A mean score of 2 on the questionnaires indicated no behavioural change after the operation;

a score above 2 indicates deterioration in behaviour and a score below 2 indicates improvement (items about positive behaviours are reverse-scored). Patients were also asked to rate their pain, before the memory test and after each postoperative behaviour questionnaire. The pain rating scale ranged from 1, no pain at all, to 5, the most pain imaginable. For children under 13 yr, the scale points were represented by schematic faces with increasingly down-turned mouths. When patients were discharged before completion of this phase of the study, the questionnaires were completed via telephone interview.

Patients completed the memory tests when they felt comfortable and able to respond to the questions. Whenever possible, testing was conducted on the day of operation. First, patients were asked a standard series of questions to determine explicit recall of the surgical period[20] (Appendix B). They then completed the word identification test, repeating any audible words from the four practice and 32 test items embedded in white noise and played over closed headphones (Sony MDR-CD170) connected to an Apple Macintosh G4 Powerbook running PsyScope software.[18]

Sample size was selected to be very large compared with previous studies using the isolated forearm technique and to give sufficient cases of awareness to detect memory priming even if it only occurred during episodes of awareness. The pilot study gave an effect size of 0.8 for the implicit memory test, and alpha was set at 0.05 throughout with one-tailed testing. If the effect size for the implicit memory test held under clinical conditions, then 12 cases of awareness should be sufficient to detect memory with power of 0.8. If Byers and Muir's[8] observed incidence of awareness (19%) held for our study, then a total sample of just 62 would be sufficient. To increase the power of our study, we aimed to recruit a sample of around 200 patients, to maintain power at 0.8 to detect memory in 19.5% of the sample with awareness even if the effect size of the implicit memory test under clinical conditions is half that estimated from the pilot study. Alternatively, a sample of 200 gives power of 0.95 to detect memory in aware patients if the effect size of the memory test is the estimated 0.8 but the incidence of awareness is only half that estimated by Byers and Muir.

Memory priming was tested using one-tailed, paired samples *t*-tests to compare target and distractor hit rates. Potential changes in anaesthetic technique or depth across the study were assessed with Pearson correlations of anaesthetic variables with participant numbers assigned to patients in test order.

Results

Written informed consent was obtained from 221 patients and their accompanying parent or carer. Of these patients, 184 (83%; 95 male and 89 female) were included in the final analysis, with data being excluded after surgery from nine patients whose surgery was completed before the study period; four patients who had learning difficulties; 23 patients who refused (e.g. because of pain) or were unable to complete the memory test on recovery (e.g. discharged before interview); and one patient who had hearing difficulties. BIS was recorded from Patient 163 onwards, operating theatre schedules permitting.

Two patients made verified responses to command on the mIFT, representing 1.09% (95% confidence interval, 0.1–3.9%) of the sample, or 0.90% of the sample including incomplete data sets. In addition, a paralysed male patient, who was subsequently excluded for not completing the memory test, made a single ambiguous response. No patient made a clear response to follow-up commands to 'squeeze your fingers twice if you are comfortable' and 'squeeze your fingers twice if you are in pain'.

Patient 10 made a verified response to the second command to move, followed by an ambiguous response to the third command. This patient was a 12-yr-old male having teeth extracted. He was paralysed (atracurium 25 μg), and received propofol 180 mg for induction and isoflurane with nitrous oxide in oxygen for maintenance of anaesthesia. End-tidal isoflurane concentration was 0.80% at the start of the study phase but had dropped to 0.65% at the time of the second command to move, approximately 1.5 SD below the mean for the patients who did not respond to command. When the patient responded to this command, the administered concentration of isoflurane was increased to re-establish an end-tidal concentration of 0.80%. On recovery, in response to the question, 'Can you remember anything in between [going to sleep and waking up]?', the patient said no but that when he was asleep he was uncomfortable and not completely unconscious or conscious. He answered no to all the specific questions about hearing words or commands. His behaviour was slightly worse at day 2 than before operation, but the change was close to the mean for the non-responders. He showed no evidence of implicit memory for the words played during surgery.

Patient 155 made a verified response to the fifth command to move. This patient was a 12-yr-old female undergoing dental extraction followed by varus osteotomy and application of an orthopaedic frame. She received sevoflurane and alfentanil 250 μg for induction, and isoflurane with nitrous oxide in oxygen for anaesthetic maintenance with caudal analgesia. Her mean end-tidal isoflurane value of 1.14% was close to the mean of 1.17% for the patients who did not respond to commands. At the fourth command, her end-tidal isoflurane concentration dropped from 1.40% to 0.95%, which is within a standard deviation of the mean for non-responders. It remained at 0.95% at the fifth command, to which she responded. Patient 155 was paralysed for intubation but was not paralysed during presentation of the mIFT commands and experimental stimuli, which happened during orthopaedic surgery. She remembered crying before going to sleep and then nothing else until recovery. Her behaviour on the day after the operation was unchanged from before the operation, and she had no implicit memory for the words played during surgery.

Table 1 shows the comparison of preoperative variables (patient characteristics and medical history) for the two patients who responded to the mIFT commands with those who did not; Table 2 shows the comparison of perioperative variables (anaesthesia and surgery); and Table 3 shows the comparison of postoperative variables (memory, pain, and behaviour).

There was no clear recall of intraoperative events, but six patients responded positively to one of the interview questions: Patient 10 recalled feeling uncomfortable while asleep, as reported above; Patient 22 remembered waking in pain with the tube still down his throat; Patient 79 responded 'yes—don't know' when asked if she remembered anything between going to sleep and waking up, but was unable to provide further details; Patient 176 responded 'no' when asked if she remembered anyone asking her to do anything with her hand or arm, but then, when asked if she remembered being asked to do anything with her right hand or arm, she said 'yes' but was not sure if it happened while she was asleep or in recovery; Patient 179 recalled hearing a train in the background; Patient 188 remembered being moved onto his side and thinking it was a dream, then recovery.

There was no evidence for intraoperative memory priming in the mIFT responders or the non-responders (Table 3). For the non-responders, the detection rate for the target words [mean (SD) of 6.91 (3.20)] was no higher than for the distractor words [mean (SD), 6.79 (3.34), P=0.25]. To check for memory priming in the most lightly anaesthetized children, target and distractor detection rates were compared for the quartile with the lowest end-tidal isoflurane (n=43, mean end-tidal isoflurane=0.83; mean target hits=6.63, mean distractor hits=6.12, P=0.052), the highest mean BIS (n=13, P=0.21), and the highest maximum BIS (n=13, P=0.08). There is therefore scant evidence for memory priming even in the most lightly anaesthetized children.

To check that anaesthetists did not alter their technique as the study progressed, anaesthetic variables were correlated with participant numbers. None of the correlations

Table 1 Preoperative variables for non-responders and responders on the modified isolated forearm technique, presented as mean (SD) (range) or percentage of sample as appropriate

Variable type	Variable	Non-responders, n=182	Patient 10: verified response	Patient 155: verified response
Patient characteristics	Age (yr) n=181	12.2 (2.8) (5–18)	12	12
	Weight (kg) n=173	49.4 (18.0) (17.2–103)	34.5	38.0
General medical history	Somewhat/very difficult experience of previous surgery	31% (57 patients)	Somewhat difficult	Somewhat difficult
	Problems with local GP/nurse	23% (41 patients)	None	Occasional

Table 2 Surgical and anaesthetic variables for non-responders and responders on the modified isolated forearm technique, presented as mean (SD) (range) or percentage of sample as appropriate

Variable type	Variable	Non-responders	Patient 10: verified response	Patient 155: verified response
Surgery	Mean length (min)	69.0 (50.3) (17–250)	150	40
Type	Orthopaedic	81%	Dental	Orthopaedic
	Dental	12%		
	Other (plastic, general, and ENT)	7%		
Premedication, analgesia, muscle relaxation	Benzodiazepine pre-medication	15%	No	No
	Caudal/epidural/local block	32%	No	Caudal
	Paralysed	36%	Yes	No
	Postop pain relief	45%	Morphine	Morphine
Induction of anaesthesia	Sevoflurane	13%		Sevoflurane+alfentanil
	Propofol	87%	Propofol	
	Co-operation (0=asleep, 4=total refusal)	1.5 (0.7) (1–4)	2–3	3
Maintenance of anaesthesia	Isoflurane+nitrous oxide	97%	Isoflurane, N_2O	Isoflurane, N_2O
	Sevoflurane+nitrous oxide	3%		
	Propofol	1 patient		
Anaesthetic variables during 17 min study period	End-tidal isoflurane (%) n=170	1.17 (0.33) (0.52–3.13)	0.73	1.14
	End-tidal CO_2 (%) n=177	5.82 (1.40) (3.60–9.22)	4.0	3.9
	Arterial pressure (mm Hg) n=175	62.1 (14.9) (35.8–115)	90.0	51.2
	Sp_{O_2} (%) n=178	98.6 (1.1) (95.0–100)	99.0	98.4
	Mean bispectral index (n=52)	37.7 (8.4) (19–56)	–	–
	Maximum bispectral index (n=52)	49.0 (9.7) (26–79)	–	–

Table 3 Postoperative variables for non-responders and responders on the modified isolated forearm technique, presented as mean (SD) (range). Behaviour change is scored as 1 for 'less than before', 2 for 'same as before', and 3 as 'more than before' for negative behaviours such as crying, and reverse scored for positive behaviours such as feeling happy. A score of 2 therefore represents no change and a score above 2 represents deterioration in behaviour since the operation

Variable type	Variable	Non-responders	Patient 10: verified response	Patient 155: verified response
Pain ratings	At memory test (n=182)	2.0 (0.92) (1–5)	3	2
	Day 2 (n=169)	2.0 (0.98) (1–5)		
	Day 7 (n=131)	1.2 (0.61) (1–5)		
Postoperative behaviour change	Day 2 (n=162)	2.08 (0.29) (1.35–3.00)	2.12	2.00
	Day 7 (n=136)	1.95 (0.24) (1.20–2.27)	2.00	Could not be contacted
Memory testing	Time to test (min) n=182	792 (525) (45–2160)	210	1080
	Priming score (difference between two proportional scores) n=182	0.01 (0.14) (−0.38 to 0.38) 95% confidence interval (−0.01 to 0.03)	−0.31	−0.13

reached significance: end-tidal isoflurane (Pearson r=0.06, P=0.40, n=184), mean BIS (Pearson r=0.02, P=0.90, n=52), maximum recorded BIS (Pearson r=0.12, P=0.39, n=52). Note that BIS was only recorded from patient number 163 onwards. There was thus no evidence that patients were more deeply anaesthetized towards the end of the study.

Discussion

Using the isolated forearm technique, modified to accommodate techniques with brief or no paralysis, this study found an incidence of intraoperative awareness in children of 1.1%. Two of 184 patients responded positively to a command to move their non-paralysed hand in the first 17 min after start of surgery, and responded again when the command was repeated. Patients were typical of the sample in terms of type of surgery (dental and orthopaedic), anaesthetic technique, and previous healthcare experiences. They were somewhat less cooperative than the sample norm, but were not totally uncooperative. Neither had adverse behavioural changes or implicit memory for words presented during surgery. One of these patients had a lower than average end-tidal concentration of isoflurane, and on recovery recalled being 'uncomfortable' and 'not completely unconscious or conscious' between induction and recovery. No variables distinguished the other patient from the non-responders.

This incidence of isolated forearm responses during surgery is much smaller than the incidence reported during tracheal intubation,[8] possibly because anaesthesia is deeper and more stable by the start of surgery. The need for multiple manoeuvres to secure the airway increases the probability of awareness.[2] The present estimate of awareness, of 1.1% of paediatric patients, is slightly higher than that reported by Davidson and colleagues.[1] Davidson and colleagues assessed awareness in patients aged 5–12 yr using detailed postoperative interviews conducted on the day or day after surgery, 3 days after surgery, and 30 days after surgery. On the basis of these interviews, seven cases were classified as 'awareness' by four independent raters, giving an estimate of awareness of 0.8% (7 out of 864 children). Another three cases were classified as 'awareness' by at least two of the four raters, and as 'possible awareness' by the others. If these cases are included, the incidence of awareness becomes 10 out of 864 children, or 1.2%. Lopez and colleagues also reported an incidence of awareness of 1.2% in a sample of 410 children aged 6–16 yr undergoing elective or emergency surgery. Cases were classified as aware if all three adjudicators rated them as 'awareness' or two adjudicators rated them as 'awareness' and the third as 'possible awareness'. Thus the mIFT and postoperative interviewing give similar estimates of the incidence of intraoperative awareness. Note, however, that the present study potentially underestimates the incidence of awareness because the isolated forearm technique was only used for 17 min from start of surgery, rather than throughout intubation and surgery. There were two reasons for restricting the period of observation. One was to relate episodes of awareness closely to memory for words presented during the episodes. The other reason was concern about keeping the cuff inflated for too long. In adults, the isolated forearm technique can be used for extended periods by briefly deflating the cuff every 20 min and then re-inflating. This was not attempted in the present study because of concerns that young children might bruise more easily than adults during extended use of the cuff.

Which technique for detecting awareness should be preferred? The mIFT gives the opportunity to increase the dose of anaesthetic and minimize the duration of the awareness episode. It is a simple technique with minimal labour, training, or equipment costs. Previous research with this technique has been restricted to paralysed patients, but this study shows, for the first time, that the structured commands of the technique, without the inflated cuff, are effective with non-paralysed patients. Thus, Patient 155 responded to commands to squeeze her hand, even though she was not paralysed and had made no movements or other signs of awareness. In the Davidson study, only four of the seven definite cases of awareness were detected from responses during the first postoperative interview. Two cases only emerged at the day 30 interview.[1] Lopez and colleagues[2] reported that one case of awareness only emerged a month after surgery, with no recall immediately post-surgery. In a large, multi-centre study of adults by Sebel and colleagues,[3] 11 of 25 cases of awareness were identified from interviews conducted in the recovery room. Fourteen cases only emerged from follow-up interviews conducted 1–2 weeks after surgery. Postoperative interviewing therefore requires extended contact with patients to detect all cases of awareness. In the present study, patients were only questioned about their memories once, on the day or day after surgery. This may explain the lack of recall of surgery even in the two children who responded to the commands to move their hand. Alternatively, the early detection and remedying of awareness afforded by the mIFT may have allowed too little time for memories to form.

The observed incidence of awareness in children is approximately eight times the incidence detected in adults through postoperative interviewing.[3] BIS recordings from a subset of children in the present study, combined with evidence of consistent anaesthetic practice over the course of the study, give no indication that children were less deeply anaesthetized than the norm. Mean end-tidal isoflurane exceeded 1 MAC and was combined with nitrous oxide. The mean BIS of 37.7 is comparable with means of 35.9 and 40.5 reported for 1 MAC isoflurane and 1.1% end-tidal isoflurane, respectively, in paediatric patients.[1 21] On average, the maximum BIS recorded for each patient (mean=49) was well below the value of around 80 associated with first awakening.[1 21] In adults, 95% of volunteers are unconscious at BIS of 50.[22] Previous research with the isolated forearm technique in adults has used much smaller samples than the present study, so further, large-scale, research is needed to establish whether adults are less prone to awareness, or less likely to recall it than children.

There was no evidence for continued memory priming during paediatric surgery, despite the large sample, although there was a trend towards memory priming in the most lightly anaesthetized children. In adults, memory priming persists when BIS below 60 indicates adequate anaesthesia,[9] but may not occur below BIS of 50.[11 23] Even small amounts of priming for neutral stimuli should alert anaesthetists to the possibility of memory formation for more salient stimuli. Note that the present sample size provides power of over 0.99 to detect the amount of memory priming observed in adults.[9] Detection of target words on the implicit memory test was actually somewhat higher than it had been in the pilot study, but detection of distractor words was considerably higher than in the pilot study. A possible explanation of this difference is that testing was carried out in a quieter setting for the main study, so that all the words on the test were easier to identify than they were in the pilot study. This difference is not likely to have affected the sensitivity of the test, because detection of distractors was still well below ceiling.

The present findings have implications for anaesthetic practice. The observed incidence of 1.1% awareness was very similar to that reported by recent studies using postoperative interviewing[1 2] but, because the mIFT allowed awareness to be detected in real time and remedied, there were minimal memory and behavioural consequences on recovery.

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Appendix A

The word lists used to test implicit memory. For a given patient, one list was played during surgery and the other provided distractor items at test.

orange	teacher
paper	apple
pond	ladder
tonight	umbrella
bucket	grass
dinner	bird
climb	stone
left	uncle
queen	dress
garden	balloon
crocodile	dance
train	castle
caterpillar	chimney
kitchen	watch
circus	before
think	holiday

Appendix B

The postoperative interview questions used to establish explicit memory for the surgical period (from Russell and Wang).[20]

Simple questions

1. What was the last thing you remember before going to sleep?
2. What was the next thing you remember?
3. Can you remember anything in between?

Cue questions

I said I would play some words to you while you were asleep.

1. Do you know what I played to you?
2. Do you remember hearing anything?
3. Do you remember anyone talking to you?
4. Do you remember anyone asking you to do anything?
5. Do you remember anyone asking you to do anything with your hand or arm?
6. Do you remember anyone asking you to do anything with your right hand or arm?

References

1 Davidson AJ, Huang GH, Czarnecki C, *et al*. Awareness during anesthesia in children: a prospective cohort study. *Anesth Analg* 2005; **100**: 653–61

2 Lopez H, Habre W, Laurençon M, Haller G, Van der Linden M, Iselin-Chaves IA. Intra-operative awareness in children: the value of an interview adapted to their cognitive abilities. *Anaesthesia* 2007; **62**: 778–89

3 Sebel PS, Bowdle TA, Ghoneim MM, Rampil IJ, Padilla MD, Domino KB. The incidence of awareness during anesthesia: a multicenter United States study. *Anesth Analg* 2004; **99**: 833–9

4 Osterman JE, Hopper J, Heran WJ, Keane TM, van der Kolk BA. Awareness under anesthesia and the development of post-traumatic stress disorder. *Gen Hosp Psychiatry* 2001; **23**: 198–204

5 Samuelsson P, Brudin L, Sandin RH. Late psychological symptoms after awareness among consecutively included surgical patients. *Anesthesiology* 2007; **106**: 26–32

6 Tunstall ME. Detecting wakefulness during general anaesthesia for caesarean section. *Br Med J* 1977; **1**: 1321

7 Kerssens C, Klein J, Bonke B. Awareness—monitoring versus remembering what happened. *Anesthesiology* 2003; **99**: 570–5

8 Byers GF, Muir JG. Detecting wakefulness in anaesthetised children. *Can J Anaesth* 1997; **44**: 486–8

9 Deeprose C, Andrade J, Harrison N, Edwards N. Unconscious auditory priming during surgery with propofol and nitrous oxide anaesthesia: a replication. *Br J Anaesth* 2005; **94**: 57–62

10 Deeprose C, Andrade J. Is priming during anesthesia unconscious? *Conscious Cogn* 2006; **15**: 1–23

11 Andrade J, Deeprose C. Unconscious memory formation during anaesthesia. *Best Pract Res Clin Anaesthesiol* 2007; **21**: 385–401

12 Wang M. The psychological consequences of explicit and implicit memories of events during surgery. In: Ghoneim MM, ed. *Awareness During Anaesthesia*. Oxford: Butterworth-Heinmann, 2001; 145–54

13 Church BA, Fisher C. Long-term auditory word priming in preschoolers: implicit memory support for language acquisition. *J Mem Lang* 1998; **39**: 523–42

14 Bonke B, Van Dam ME, Van Kleef JW, Slijper FME. Implicit memory tested in children during inhalation anaesthesia. *Anaesthesia* 1992; **47**: 747–9

15 Kalff AC, Bonke B, Wolters G, Manger FW. Implicit memory for stimuli presented during inhalation anesthesia in children. *Psychol Rep* 1995; **77**: 371–5

16 Rich JB, Yaster M, Brandt J. Anterograde and retrograde memory in children anesthetized with propofol. *J Clin Exp Neuropsychol* 1999; **21**: 535–46

17 Edwards RPA, Gibbon V. *Words Your Children Use*. London & Toronto: Burke Books, 1973

18 Cohen JD, MacWhinney B, Flatt M, Provost J. PsyScope: a new graphic interactive environment for designing psychology experiments. *Behav Res Methods* 1993; **25**: 257–71

19 Kotiniemi LH, Ryhänen PT, Moilanen IK. Behavioural changes in children following day-case surgery: a 4-week follow-up of 551 children. *Anaesthesia* 1997; **52**: 970–6

20 Russell IF, Wang M. Absence of memory for intra-operative information during surgery under adequate general anaesthesia. *Br J Anaesth* 1997; **78**: 3–9

21 Whyte SD, Booker PD. Bispectral index during isoflurane anesthesia in pediatric patients. *Anesth Analg* 2004; **98**: 1644–9

22 Glass PS, Bloom M, Kearse L, *et al*. Bispectral analysis measures sedation and memory effects of propofol, midazolam, isoflurane, and alfentanil in healthy volunteers. *Anesthesiology* 1997; **86**: 836–47

23 Stonell CA, Leslie K, He C, Lee L. No sex differences in memory formation during general anesthesia. *Anesthesiology* 2006; **105**: 920–6