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Implicit Memory Formation during Routine Anesthesia in Children

A Double-masked Randomized Controlled Trial

Xiuzhi Pham, B.Med.Sc.,* Katherine R. Smith, B.Sc.(Hons), M.Biostat.,†
Suzette J. Sheppard, B.Sc.(Hons),‡ Carolyn Bradshaw, B.Bus.Comp., G.Dip.Psych.,§
Eric Lo, B.Med.Sc.,* Andrew J. Davidson, M.B.B.S., M.D., F.A.N.Z.C.A.‖

ABSTRACT

Background: Implicit memory cannot be consciously recalled but may be revealed by changes in behavior. There is evidence for implicit memory formation during anesthesia in adults, but several studies in children have found no evidence for implicit memory. This may be due to insensitive testing. Also many of these tests were undertaken under controlled conditions. It remains unknown whether implicit memory is formed during routine pediatric anesthesia. The aim of this study was to determine whether there is evidence of implicit memory formation during routine anesthesia in children, using a degraded auditory stimulus recognition task.

Methods: Three hundred and twelve children, aged 5–12 yr, were randomly assigned to be played either a sheep sound or white noise continuously through headphones during general anesthesia. No attempt was made to standardize the anesthetic. On recovery, children were played a sheep sound degraded by a white noise mask that progressively decreased over 60 s, with the outcome being the time taken to correctly recognize the sheep sound.

Results: Three hundred children completed the task. A comparison of the distribution of recognition times between the two groups found little evidence that exposure to a sheep sound during anesthesia was associated with postoperative time to recognition of a degraded sheep sound (hazard ratio 1.14, 95% CI of 0.90–1.43, $P = 0.28$).

Conclusion: No implicit memory formation during routine anesthesia was demonstrated in children. It is increasingly likely that the potential clinical implications of implicit memory formation are less of a concern for pediatric anesthetists.

What We Already Know about This Topic

- ❖ Implicit memory, which alters behavior but cannot be consciously recalled, may be formed in adults, but there is no evidence that it is formed in children during general anesthesia
- ❖ Whether this difference reflects small sample sizes and highly controlled conditions in studies in children is uncertain

What This Article Tells Us That Is New

- ❖ In more than 300 children given general anesthesia in routine practice, there was no evidence for implicit memory formation during anesthesia

IMPLICIT memories are memories that cannot be consciously recalled but can still have an influence on feelings, thoughts, and behavior. Although the relevance of implicit memory during anesthesia is unclear, it has been suggested that it may contribute to problematic behavior after anesthesia.[1] There is evidence for the formation of implicit memory during anesthesia in adults.[2] In contrast, it is less clear whether children can form implicit memories during anesthesia. It is plausible that implicit memories are formed in children during anesthesia as compared with explicit or consciously recalled memory, and implicit memory emerges early in life and is thought to be developmentally stable from the age of 3.[3,4] It is perhaps also pertinent that there is an increasing evidence that explicit memory formation during anesthesia (awareness) is greater in children than in adults.[5–9] Nevertheless, published pediatric studies have detected no or only weak evidence for implicit memory formation during

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* Student Researcher, Department of Paediatrics, University of Melbourne, Parkville, Victoria, Australia, and Anaesthesia Research Group, Murdoch Childrens Research Institute, Parkville, Victoria, Australia. † Statistician, Clinical Epidemiology and Biostatistics Unit, Murdoch Childrens Research Institute. ‡ Project Coordinator, § Research Assistant, Anaesthesia Research Group, Murdoch Childrens Research Institute. ‖ Clinical Associate Professor, Department of Paediatrics, University of Melbourne, and Department of Anaesthesia, Royal Children's Hospital, Parkville, Victoria, Australia.

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Address correspondence to Dr. Davidson: Department of Anaesthesia, Royal Children's Hospital, Flemington Road, Parkville 3052, Victoria, Australia. andrew.davidson@rch.org.au. This article may be accessed for personal use at no charge through the Journal Web site, www.anesthesiology.org.

anesthesia.[1,10–14] These negative findings may be attributable to various methodological limitations, such as small sample sizes, lack of a formally constructed control group, using memory tasks with only limited validation, and testing for the more complex conceptual priming rather than perceptual priming. Also, the auditory priming stimuli may have been unfamiliar, too numerous or presented for too short a duration, and reliance on dichotomous outcome measures may have further decreased the sensitivity of these studies. Some of these studies also tested for implicit memory only during prescribed anesthesia conditions. Although it is interesting to identify implicit memory in such prescribed conditions, it may be worthwhile to first investigate whether there is any evidence for implicit memory formation in everyday routine pediatric anesthesia.

We recently developed a new test of perceptual priming to detect implicit memory suitable for children in the setting of anesthesia; the degraded auditory stimulus recognition task.[15] The aim of this study was to determine whether there was evidence for implicit memory formation during routine anesthesia in children, using this perceptual priming task.[15]

Materials and Methods

This randomized, double-blinded controlled trial was conducted at the Royal Children's Hospital in Victoria, Australia, with ethical approval granted by the institution's Human Research Ethics Committee and written informed consent from parents or guardians. Children aged 5–12 yr scheduled for general anesthesia were considered for inclusion. Children were excluded if they were hearing impaired, developmentally delayed, nonEnglish speaking, expected to be mechanically ventilated postoperatively, having procedures that precluded use of headphones, or involved in previous studies in which sounds were played.

Randomization and Blinding

Children were randomized using a sequentially numbered, opaque, sealed envelope system to be played either one of two compact discs (CD, "A" or "B") in a 1:1 ratio, using a variable block size. The randomization schedule was generated using Stata version 10.0 (Stata Corporation, College Station, TX). Randomization was stratified according to age (5 to <9 yr and 9 to <13 yr), as the study by Phelan *et al.*[15] showed a strong association between age and test performance.

The CDs used in this study were identical to those used in the study by Phelan *et al.*[15] One CD contained a 60-s recording of a sheep sound whereas the other contained a 60-s recording of white noise. An independent statistician arbitrarily labeled these as either "A" or "B". The study investigators and the statistician were unaware of which CD corresponded to which sound. After the patient was entered into the study, the randomization envelopes were opened sequentially by a researcher, and the allocation was recorded on patient case report forms. Others involved (anesthetists, surgeons, participants and their parents) were unaware of this allocation and also of what the intraoperative sounds actually were.

Procedure

Prospective candidates were identified from daily theater schedules and approached before anesthesia. Written informed parental consent and verbal child assent were obtained before enrolment. To avoid inducing anxiety in children concerning the possibility of memory formation during anesthesia, parents, anesthetists, and others involved in the study were requested not to tell the children that sounds would be played during anesthesia. A preoperative trial of the degraded auditory recognition task using a cat sound was also performed to check the hearing and cognitive ability of the child, to familiarize them with the task and researcher, and to set the volume level for subsequent use.

Treating anesthetists were permitted to give the anesthetic and other agents at their discretion and to use anesthesia depth monitoring if desired. Headphones were placed on the child, and the assigned CD played after induction of anesthesia, immediately before insertion of the laryngeal mask airway or the endotracheal tube. The track was played on repeat and stopped when anesthesia ended (cessation of volatile agent or total intravenous anesthesia), unless clinical circumstances arose that necessitated removal of the headphones. The start and end times of the exposure were recorded.

Demographic data were obtained from patients and medical records. In addition, anesthesia and surgical information were collected. This included administration of any sedative premedications, induction and maintenance agents, muscle relaxants, and intraoperative analgesics. The end-tidal concentrations of maintenance agents were noted at 5-min intervals throughout the procedure.

Postanesthesia, the children were interviewed and tested when they were orientated and willing to participate. This was on the day of surgery where possible, otherwise on the following day. First, any explicit memory or dreaming was elicited using a structured interview as described previously.[9] The children were then played the degraded auditory recognition task with a cow sound that, similar to the preoperative cat trial, was intended to familiarize children with the test. The implicit memory test with the degraded sheep sound was then administered. Finally, the children were told that sounds had been played during anesthesia, and the purpose of the study was explained.

The primary outcome was time to unprompted recognition of a sheep sound, measured in seconds, on the degraded sheep auditory stimulus recognition task. Responses accepted as correct were "sheep," "lamb," "goat, " or "baa."

The Degraded Auditory Stimulus Recognition Task

The degraded auditory stimulus recognition task involves playing a 60-s track of mixed sound to a child. The track starts with 100% white noise and over 60 s the amount of white noise in the mix decreases to zero whereas the amount of the recognizable sound (such as a sheep) increases from none to pure sound. Children are timed as to how quickly they can identify the sound because it gradually becomes clearer over the 60 s. If children have been exposed to the sound previously, they will recognize it faster, even when they have no recollection of having heard it before.[15]

Sample Size

In the study by Phelan *et al.* with 105 children, priming was demonstrated for a sound played before anesthesia with an estimated hazard ratio of 2.2 (unreported calculation obtained from survival analysis of the study data). As the current study would involve priming of a sound during actual anesthesia, a more modest effect size was anticipated. It was considered feasible for about 300 patients to be recruited into the study, which would permit detection of a hazard ratio of 1.4 with 80% power at a 5% significance level. This calculation assumed a censoring rate (probability of not recognizing the sound within 60 s) of 10% in the control group, based on the control group censoring rate in the pilot.

Statistical Methods

The time-to-recognition distributions of the two randomization groups were displayed graphically using Kaplan-Meier failure curves. Cases where explicit memory of hearing the sheep sound was reported were to be excluded from analysis. Observations were censored if the child failed to recognize the sound by the end of the track, stopped listening partway through, or recognized the sound only upon prompting.

Proportional hazards regression was used to compare the instantaneous probability of sheep sound recognition at any moment during the task between the two groups. Estimates were expressed as hazard ratios with associated 95% CIs. The Efron method was used to handle ties and the proportional hazards assumption was checked for all such analyses, both visually and by testing for a constant log-hazard ratio overtime.[16]

The prespecified analysis plan was an intention-to-treat analysis with the randomization group as the only covariate. A per protocol sensitivity analysis was also performed with the sound actually heard, rather than allocated. A further analysis was performed to investigate the effect of adjusting for two covariates that the researchers *a priori* considered likely to be associated with the primary outcome, namely the age of the child and the duration of anesthesia (reflecting the amount of time for which a child was exposed to the sound played intraoperatively). Interactions of each covariate with the randomization group were considered and retained if they yielded $P \leq 0.05$. Model fit was investigated by plotting Cox-Snell residuals against their cumulative hazard.

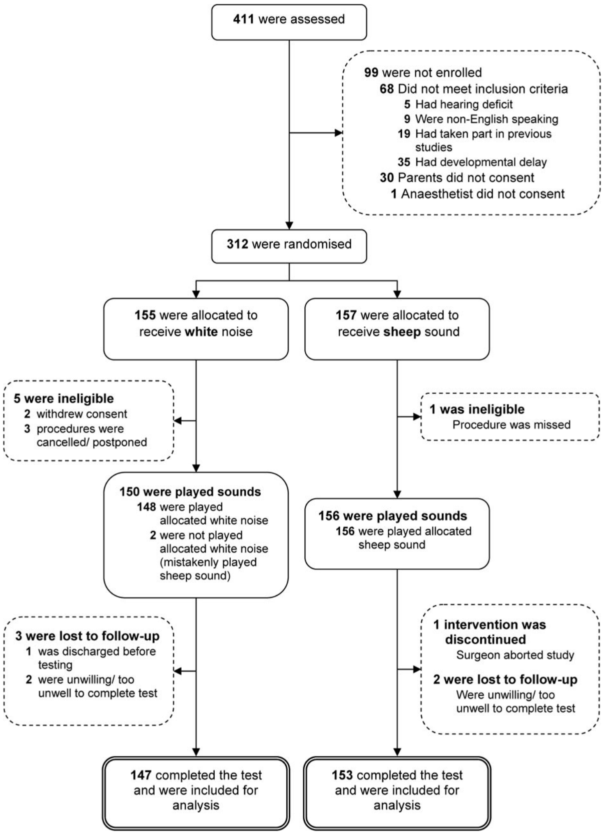


Fig. 1. Flow of participants in the study.

During peer review of the manuscript, it was also suggested that measures of anesthesia depth were investigated as possibly important covariates. Therefore, we performed two further *post hoc* analyses, one adjusting for presence of possible awareness or dreaming and another adjusting for end-tidal concentration of anesthetic. The end-tidal concentration of anesthetic was calculated by adding the age-adjusted minimum alveolar concentration (MAC) equivalents for end-tidal concentrations (where applicable) of isoflurane, sevoflurane, and nitrous oxide for each recorded time period (every 5 min) while the sound was played. These were then averaged for each child. The age-adjusted MAC equivalents were calculated using the formulae described by Lerou.[17] For each model, we included the randomization group and age as well as the new covariate of interest. Each model included an interaction term for the covariate with randomization group, because it seemed plausible that the effects of anesthesia depth upon time to recognition of sheep sound might differ between the sheep and white noise groups.

Other data were summarized using appropriate descriptive statistics (mean and SD for normally distributed or symmetric variables; median and interquartile ranges for skewed variables; number and proportion for categorical variables). All analyses were performed using Stata 10.0 (StataCorp LP, College Station, TX).

Results

Details about the number of children assessed for eligibility, excluded, and randomly assigned to hear either the sheep sound or white noise are shown in figure 1. A total of 312 children were enrolled between September 2008 and March 2009, with 12 of these being additional recruitments to replace children who were enrolled but did not receive the

Table 1. Demographic Data by Randomization Group

Characteristic	White Noise (n = 147)	Sheep Sound (n = 153)
Age, yr	8.9 (2.3)	9.0 (2.2)
Gender, male	82 (56%)	87 (60%)
Weight, kg	32.4 (12.0)	32.0 (10.9)
Previous anesthetic	109 (74%)	107 (70%)
Chronic illness(es)	67 (46%)	60 (39%)

Categorical data are expressed as n (%). Continuous data are reported as mean (standard deviation).

intervention (n = 6) or who did not complete the implicit task (n = 6). Two children randomized to the control group were played the sheep sound by mistake; all other children were played their allocated sounds. Five children who correctly recognized the sheep sound did so after nondirective prompting by the tester, which was not specified in the protocol. The final sample for analysis consisted of 300 children.

Reasonable balance was achieved with regard to age, sex, procedure performed, and anesthesia details (tables 1 and 2). However, in spite of randomization, on inspection there was evidence for an imbalance in duration of surgery, with the sheep group experiencing longer median durations of surgery and hence anesthesia and exposure to sound (table 3). It was not possible to conduct the postoperative interview and task on the day of surgery in 20 instances (white noise: n = 7; sheep: n = 13). The overall median time difference between the end of anesthesia and the interview was similar between groups (1.4 *vs.* 1.5 h). The rate of censoring was approximately 3% for the sheep group and 6% for the white noise group. Because no child had explicit recall of a sheep, no child needed to be excluded from the analysis for implicit memory formation because of explicit memory formation.

Figure 2 shows Kaplan-Meier failure curves for the time to recognition in the two groups. Median time to recognition was 22 s for both groups. The primary analysis yielded little evidence ($P = 0.28$) that exposure to a sheep sound during anesthesia was associated with postoperative time to recognition of the degraded sheep sound. The hazard ratio for sheep recognition was estimated to be 1.14, with a 95% CI of 0.90–1.43. In other words, children allocated to hear the sheep sound intraoperatively were estimated to be 1.14 times more likely than the children allocated to hear white noise to recognize the sheep sound at any moment during the implicit memory test, given that they had not yet recognized the sheep sound before that moment. In the underlying population, the hazard may be up to 10% lower or up to 43% higher for the sheep group compared with the white noise group. The CI includes the null value of 1, corresponding to the equal probability of recognition for both groups. The sensitivity analysis with the per-protocol analysis yielded results essentially the same as that of the primary analysis with a hazard ratio of 1.15 (95% CI 0.91–1.45, $P = 0.24$).

Table 2. Perioperative Data by Randomization Group

Characteristic	White Noise (n = 147)	Sheep Sound (n = 153)
Surgery		
Orthopedic	38 (26)	45 (29)
Gastroenterology	40 (27)	35 (23)
General Surgery	23 (16)	25 (16)
Plastics and maxillofacial	19 (13)	14 (9)
Urology	9 (6)	15 (10)
General medicine	9 (6)	5 (3)
Hematology	4 (3)	7 (5)
Oncology	4 (3)	5 (3)
Burns	0	1 (0.7)
Gynecology	0	1 (0.7)
Respiratory	1 (0.7)	0
Emergency cases	1 (0.7)	3 (2)
Sedative premedication	10 (6.8)	12 (7.8)
Induction		
Inhalation	83 (57)	77 (50)
Inhalation and intravenous	64 (44)	76 (50)
Airway management		
Laryngeal mask airway	122 (83)	113 (74)
Endotracheal tube	7 (5)	24 (16)
Face mask only	13 (9)	14 (9)
LMA, followed by ETT	5 (3)	1 (0.7)
Nasal cannula	0	1 (0.7)
Maintenance		
Sevoflurane only	50 (34)	55 (36)
Sevoflurane + N_2O	40 (27)	24 (16)
Isoflurane only	30 (20)	45 (29)
Isoflurane + N_2O	26 (18)	27 (18)
Propofol infusion	1 (0.7)	1 (0.7)
Propofol infusion + sevoflurane	0	1 (0.7)
Other agents bolus during maintenance		
Propofol	22 (15)	27 (18)
Midazolam	5 (3)	5 (3)
Ketamine	5 (3)	5 (3)
Clonidine	2 (1)	0
Muscle relaxants	3 (2)	7 (5)
Analgesia		
Intraoperative opioids	59 (40)	71 (46)
Local anesthesia	66 (45)	78 (51)
Opioids given in PACU	11 (8)	22 (15)

Categorical data are expressed as n (%).

ETT = endotracheal tube; LMA = laryngeal mask airway; PACU = postanesthesia care unit.

Evidence for a priming effect weakened further after adjustment for child age (modeled as a continuous covariate). The age-adjusted hazard was estimated to be 8% higher for the sheep group (95% CI of 15% lower to 36% higher hazard, $P = 0.54$). A strong evidence was found for age being associated with the hazard of sheep sound recognition ($P < 0.001$), with the hazard of correctly recognizing the sheep sound estimated to increase by 12% for each increase in age of 1 yr (95% CI of 6% increase to 18% increase). Little evidence was found for an age by randomization group in-

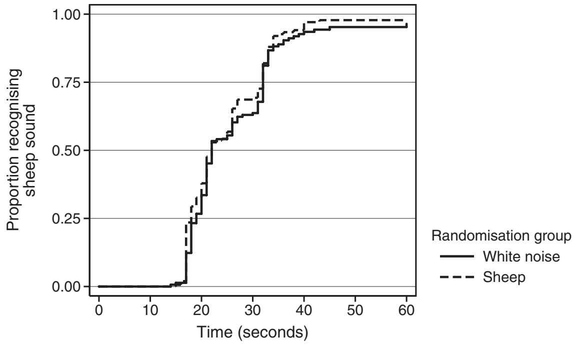
Table 3. Time Data by Group

Times	White Noise (n = 147)	Sheep Sound (n = 153)
Duration of surgery (min)	14 (9–25)	19 (8–37)
Duration of anesthesia (min)	26.0 (19.0–39.5)	34 (20–53)
Duration of transfer from induction room to operating room (s)	33.5 (26.0–44.5)	37.0 (28.5–49.0)
Duration of exposure (min)	23 (16–35)	31 (18–50)
Time between induction and start of exposure (min)	3 (2–3)	2 (2–3)
Time between the end of anesthesia and interview (h)		
Same day interview, n = 280	1.4 (1.0–1.8)	1.4 (1.0–2.0)
Next day interview, n = 20	19.4 (16.8–20.5)	16.9 (16.6–20.3)

Times are reported as median (interquartile range).

teraction ($P = 0.16$). When duration of anesthesia (modeled as the base 2 logarithm of time in minutes) was added to the age-adjusted model, no evidence was found for an association with the hazard of correctly recognizing the sheep sound ($P = 0.23$). The proportional hazards assumption was checked and found to be reasonable for all models ($P \geq 0.48$ for a null hypothesis of a constant log-hazard ratio). Model fit was investigated for the age-adjusted model and found to be satisfactory.

For estimating average MAC equivalent of end-tidal concentrations, there were data for 128 children in the white noise group and 144 in the sheep sound group (data were missing in some children and those who received total intravenous anesthesia were excluded). The mean average MAC equivalent of end-tidal concentration was 1.30 (SD 0.37) for the white noise group and 1.25 (SD 0.47) for the sheep sound group. Adding MAC equivalent and an interaction with group to the age-adjusted model did not strengthen the evidence for an association between group and the primary outcome, with a Wald test of the hypothesis that the hazard ratios for group and the group-MAC equivalent interaction are jointly one (have no effect), yielding $P = 0.52$. The hazard ratio for the group-MAC equivalent interaction was 1.27 (95% CI 0.68–2.38).



Number at risk							
White noise	147	147	107	54	9	4	4
Sheep	153	153	103	47	8	3	3

Fig. 2. Kaplan-Meier failure curves for the time to recognition of the degraded sheep sound in the two groups.

Twenty-two children (14.9%) reported dreaming during anesthesia, 12 in the white noise group, and 10 in the sheep sound group. Six children (2%) reported memories in the interview that suggested possible intraoperative awareness, five of the six in the white noise group and one in the sheep sound group. One child in the white noise group reported both a dream and memories, which were possibly awareness. Characteristics of possible awareness are described in table 4. None of the possibly aware children reported feeling frightened or distressed about the experience.

Adding possible awareness or dreaming and an interaction with group to the age-adjusted model did not strengthen the evidence for an association between group and the primary outcome, with a Wald test of the hypothesis that the hazard ratios for group and the group-possible awareness or dreaming interaction are jointly one (have no effect), yielding $P = 0.25$. The hazard ratio for the group-awareness/dreaming interaction was 1.91 (95% CI 0.83–4.38).

Discussion

This study found no evidence of implicit memory formation in children during routine anesthesia. This result is consistent with previous studies. By using perceptual priming, Andrade *et al.*[10] and Lopez *et al.*[1] also found no evidence of implicit memory in children during anesthesia, although their findings may have been influenced by their use of multiple stimuli and relatively few presentations. We primed children with only one stimulus played continuously after induction until the cessation of anesthesia. Bonke *et al.*[11] and Kalff *et al.*[12] also found no evidence for priming. However, in their studies there were study-test changes in modality, which may have reduced the likelihood of priming.[18]

A significant difference between our study and previous studies was also that in our study there was no standardization of anesthesia delivery or anesthesia depth. The anesthetic regimen was left to the discretion of the treating anesthetist. The reason for doing this was that we wished to determine whether implicit memory is formed during routine or real life pediatric anesthesia. In this respect, this study is more of an observational study rather than a study specifically addressing the question of whether or not age influences the likelihood of implicit memory at any particular dose or depth of anesthesia. Anesthesia practice differs somewhat between adults and children, thus we believed that it is important to determine whether indeed implicit memory is

Table 4. Possible Awareness Cases

Age	Sex	Group	Procedure	Induction, Maintenance, Other	Explicit Memory
5 yr 1 mo	Male	White noise	Joint injections	I: Propofol + sevoflurane + N_2O M: Isoflurane + N_2O	Child recalled "feeling needles, everywhere" and also ringing in the ears.
7 yr 8 mo	Male	White noise	Change of vacuum dressing on arm	I: Sevoflurane + N_2O M: Sevoflurane + N_2O O: Ketamine premedication	Was certain about hearing something but could not remember what it was.
8 yr 9 mo	Male	White noise	Gastroscopy	I: Sevoflurane + N_2O M: Sevoflurane only	Reporting hearing a "fuzzy" sound "in the middle" for "a few seconds". Thought it sounded like a broken television.
9 yr 3 mo	Male	White noise	Percutaneous endoscopic gastrostomy	I: Sevoflurane + N_2O M: Sevoflurane	Described feeling the "tube" being removed and replaced in his stomach and hearing people "asking for stuff." Later clarified hearing this as he was going off to sleep.
9 yr 5 mo	Male	White noise	Plastic surgery to hand	I: Propofol + sevoflurane + N_2O M: Isoflurane + N_2O O: Clonidine	Child recalled hearing a fuzzy noise after told during debriefing that headphones had been placed on him (but not what sounds were played) while asleep. Also dreamt of being Batman.
10 yr 1 mo	Male	Sheep	Gastroscopy	I: Sevoflurane + N_2O M: Sevoflurane + N_2O	"Feeling something going into hand," "About 1/4 of the way through;" Later said it was a needle.

I = induction; M = maintenance; O = other.

formed during routine anesthesia in children before embarking on more rigorous and challenging studies to determine whether there is a specific effect of age.

Studies in adults have found evidence for implicit memory formation during anesthesia. It is unclear why there is some evidence for implicit memory formation during anesthesia in adults but not in children. This may be because of the possible differences with age in memory formation or the pharmacology of general anesthetics. However, there are several other possible reasons for this discrepancy of findings. First, the hospital experience can be distressing and confusing for children. Thus, when testing memory, children may be more reticent and less cooperative than adults, particularly after an experience such as surgery. Second, it is possible that implicit memories are indeed formed in children during anesthesia, but to such a small extent that it remains undetected with any of the current tests used in children. In other words, despite the successful validation on pilot studies, tasks that have been used may still lack the sensitivity to detect the level of implicit memory formation that takes place during anesthesia in children. Lastly, the emotional salience of the stimulus may also influence priming. Comments with great negative connotations or personal relevance may be more likely to lead to implicit memory.[19] The stimuli used in tests for children have not been emotionally charged. The use of more salient stimuli may be a consideration for future studies.

There are particular reasons why implicit memory may not have been detected in our study. The mean average end-tidal MAC equivalent during sound exposure in this study was more than 1.25 MAC. There is some evidence that in adults implicit memory formation tends to be more likely during light anesthesia.[2] Although MAC equivalent data are imperfect for the reasons explained previously and direct comparisons with studies in adults are difficult because of differences in design and outcome measure, it could be argued that 1.25 MAC is relatively deep anesthesia and this may explain the lack of implicit memory formation in our study compared with studies performed in adults.

Although the findings add weight to the evidence that implicit memory does not form during anesthesia in children, our negative results should also be considered in the light of several other possible study limitations. First, to ensure the detection of an effect that may diminish with time, implicit memory testing should be conducted as soon as possible after surgery. Twenty children were too unwell to be interviewed on the day of surgery; however, the median time interval for testing the next day was 18 h, well within the 36-h interval advocated by Merikle and Daneman in their meta-analysis of studies with adults.[20,21]

Second, there was, on inspection, a degree of imbalance between groups in our study with a greater proportion of children randomized to the sheep group having longer surgery. It is difficult to predict how the priming effect may have been affected by any imbalance. When the analysis was adjusted for duration of surgery, there was still no evidence for implicit memory formation.

Third, although anesthetists and other healthcare staff were blinded to the randomization and unaware of the possible sounds, they did know which children were enrolled in the study. It is possible that an anesthetist might err on the side of deeper anesthesia if they knew a child was in a study that involved memory assessment. This cannot be proven or disproven; however, it is interesting to note that in recent studies of awareness in the same institution, the rate was higher when the anesthetist was unaware that an awareness study was underway.[5,9] Related to this issue, in this study anesthesia depth monitoring was not used. Such monitoring is not a routine practice at our institution, and it was not added to the study protocol for logistic reasons. Without a measure of anesthesia depth, it is difficult to know how deeply anesthetized children were in this study and hence how to generalize the findings to other populations. The use of depth monitoring may also be useful to specifically investigate the influence of anesthesia depth on memory formation; and certainly future studies should strive to include depth monitoring.

Lastly, the lack of standardization did lead to some variation in the type and depth of anesthesia. However, end-tidal concentrations of volatile anesthesia were recorded, allowing some analysis of the effect of anesthesia dose on implicit memory formation. There was no evidence for implicit memory when adjusted for anesthesia dose, but it is important to note that the study was not powered or specifically designed to test this association and this was a *post hoc* analysis. Similarly, there was no evidence for an interaction between dose and randomization group. However the CIs around this interaction were wide, so the possibility that such an interaction might exist cannot be ruled out. It should also be noted that the data on anesthesia dose are imperfect; records were only made every 5 min and there was no adjustment for use of boluses of propofol during maintenance or the use of opioids. Also, memory may occur during brief periods of lighter anesthesia and that averaging data every 5 min may not detect these brief periods of lighter anesthesia. A further *post hoc* analysis was suggested to investigate dreaming and possible awareness as potential markers of light anesthesia. As for anesthesia dose, when adjusting for dreaming and possible awareness, there was no evidence for an association with response time and there was no evidence for an interaction; however the total number of dreaming and awareness events was small, thus limiting the power of this analysis.

In this study, we sought to detect children with clear explicit memory of the sheep sound so that we could exclude them from analysis. The study was not designed primarily to assess dreaming or awareness; however, our observed overall incidence of dreaming (7.3%) was similar to that reported by *Huang et al.*,[22] (10.4%) and the incidence of "possible awareness" was similar to the "preadjudicator reports" in other studies (1.5[7] to 2.2%[5]). Importantly, there was no independent adjudication of awareness and only one interview was conducted; thus, we cannot comment on the "true" rate of awareness in this study.

In conclusion, we found no evidence for implicit memory formation during anesthesia in children. Although implicit memory tests are not without limitations, this result does add to the increasing body of evidence suggesting implicit memory formation is unlikely to be relevant to pediatric anesthesia.

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ANESTHESIOLOGY REFLECTIONS

A Mountain Gorge by D. E. Jackson

Vocationally, pharmacologist Dennis Emerson Jackson, M.D. (1878–1980), pioneered absorption of carbon dioxide from circle breathing systems. Avocationally, as an artist, Jackson enjoyed painting landscapes, including *A Mountain Gorge* in 1937 in oil on wood (*above,* courtesy of the Wood Library-Museum). He displayed this oil painting at the San Francisco Museum of Art the following year as a member of the American Physicians Art Association, a nonprofit group that Jackson supported for the next 40 yr. A year after he received the American Society of Anesthesiologists' Distinguished Service Award in 1963, Jackson observed that his artworks "show that anesthesiologists do not live by bread alone, but that they are really very human people." (Copyright © the American Society of Anesthesiologists, Inc. This image appears in color in the *Anesthesiology Reflections* online collection available at www.anesthesiology.org.)

George S. Bause, M.D., M.P.H., Honorary Curator, ASA's Wood Library-Museum of Anesthesiology, Park Ridge, Illinois, and Clinical Associate Professor, Case Western Reserve University, Cleveland, Ohio. UJYC@aol.com.