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Psychological Effects of General Anesthesia on Five- to Eight-year-old Children

Steven F. Morgan, Ph.D., Eric B. Furman, M.D.,† Sureyya Dikmen, Ph.D‡*

Thirty-six five- to eight-year-old children undergoing routine myringotomy procedures and maintained with halothane-N_2O general anesthesia (mean duration = 17.9 min) were administered a series of psychological performance measures prior to and at about two hours after surgery. A control group of 30 children not experiencing anesthesia or surgery was tested at comparable intervals. In addition, 16 of the anesthesia group and 15 of the control group subjects were retested again the next day, about 24 h postsurgery. The anesthesia group demonstrated impairment on tests of reasoning, motor and memory functions at two hours postanesthesia. There was no evidence for continued impairment 24 h later. The effects at two hours postanesthesia did not appear related to induction medication or group differences in discomfort/symptomatology. (Key words: Anesthesia: pediatric; outpatient. Anesthetics, gases: nitrous oxide. Anesthetics, intravenous: thiamylal. Anesthetics, volatile: halothane. Memory. Psychologic responses. Recovery.)

ADULTS MAY SHOW IMPAIRMENT of psychological functioning for varying periods of time after exposure to general anesthesia.[1-7] Comparable studies with children have not been reported. An assessment of the psychological effects of anesthesia on children is important because of the many physical, developmental, and psychological differences between adults and children which make it a questionable assumption that a child's behavior will be affected by anesthesia in the same way as an adult's behavior. Since children are in general unable to articulate complaints of impaired psychological functioning, clinical observation or interviews alone may give an inaccurate impression of the degree of recovery after anesthesia. This study utilizes formal psychological measures to assess the pattern and duration of intellectual and adaptive impairment, if any, in five- to eight-year-old children following a minor surgical procedure maintained with halothane-N_2O general anesthesia.

Materials and Methods

The subjects were two groups of five- to eight-year-old children. The anesthesia group consisted of 36 children (19 male, 17 female) with a mean age of 6.8 yr (SD = 1.4 yr) who were given general anesthesia while undergoing myringotomy procedures at The Children's Orthopedic Hospital in Seattle, Washington. These children were selected for the anesthesia group because they were in good health and were expected to be in minimal physical discomfort both prior to and after the procedure. Subjects in the control group, which was included to control for learning effects on the measures across the test periods, were 30 children (15 male, 15 female) with a mean age of 6.9 yr (SD = 1.2 yr). These children were administered the same psychological measures as the anesthesia group at their preschools and elementary schools in suburban Seattle. A group to directly control for any potential performance effects of hospitalization was not included because other children experiencing brief hospitalization were quite disparate from the anesthesia group subjects on several factors which can influence psychological test performance. Other hospitalized children tended to be in greater pain and discomfort, in poorer general health, and were often receiving psychoactive medications. Therefore, as an alternative to direct control, measures relevant to potential hospitalization effects (*e.g.*, physical discomfort, nervousness) were administered to subjects in both the anesthesia and control groups so that any group differences on these measures could be controlled statistically.

PROCEDURE

None of the anesthesia subjects was premedicated. Of the 36 anesthesia patients, 14 had rectal thiamylal induction (25 $mg \cdot kg^{-1}$) and 11 had intravenous thiamylal induction (4–5 $mg \cdot kg^{-1}$). The remainder had inhalation induction with halothane-N_2O anesthesia. Rectal induction tended to be performed with the youngest patients and intravenous induction with the oldest, with the choice of technique depending on the individual anesthetist's perception of the child's needs. Atropine was given to six of the children to dry secretions. Each child was given Ringer's lactate solution intravenously at a rate of 4 $ml \cdot kg^{-1} \cdot h^{-1}$. Anesthesia was maintained for all the patients with halothane (1.5–2.5 per cent) in 60 per cent nitrous oxide and oxygen. No child had endotracheal intubation, and all children breathed spontaneously. The duration of anesthesia ranged from 10 to 35 min (mean = 17.9 min, SD = 6.8 min). Following surgery, the children were taken to the recovery room where they were given 30 per cent oxygen for a minimum of 15 min. None of

* Postdoctoral Fellow, Psychiatry Research Unit, University of Minnesota, Minneapolis, Minnesota.

† Director, Department of Anesthesiology, The Children's Orthopedic Hospital, Seattle, Washington.

‡ Assistant Professor, Department of Rehabilitation Medicine, University of Washington, Seattle, Washington.

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the subjects required analgesic medication postoperatively.

The series of dependent measures was administered to children in the anesthesia group approximately 2.5 h before surgery, at the time of discharge from the hospital (mean time = 128 min postsurgery; SD = 40 min) and again approximately 24 h later. The presurgical testing took place after the child had been admitted to the Short Stay Unit and had received the standard presurgical medical care and examination. The first postsurgical testing took place when the medical staff had determined that the child was able to keep down liquids and ambulate. Because of living long distances from the hospital or because both parents were working the following day, only 16 of the 36 anesthesia subjects were available for the 24-h follow-up testing. For the control group, subjects were individually administered the dependent measures at time intervals comparable to that for the anesthesia group. All control subjects were tested at the first two test periods, and 15 of the 30 control subjects were randomly selected for the 24-h follow-up testing. For both groups, the testing was individually administered in small, quiet rooms without other persons present. For all subjects in the study, the order in which the tests were administered was counterbalanced across the subjects. For each subject individually, however, the tasks were given in the same order at each test period. An exception to the counterbalancing was that the Selective Reminding task was always administered first so that the time period prior to the delayed recall portion of that task, which was always administered last in the series of tests, would be maximized. At the end of each test period, each child was allowed to select a small toy or book as a gift for doing his/her best. This was for the purpose of encouraging maximum effort and performance. It was impossible to test the children without an awareness of the particular test period and group membership of the subject. Objectivity of measurement was partially protected by the use of tests with clear and objective scoring criteria.

Dependent Measures

The dependent measures used in this study were grouped into two categories: 1) measures of intellectual-adaptive performance (listed and described in table 1), and 2) measures of symptoms and behavior. Two measures of symptoms and behavior were included. The Symptom Rating Scale (SRS) was administered to each child in the study at each test period. The SRS was derived for the present study from the Symptom Checklist used by Davison and colleagues with adult subjects.[2] The six items which contribute to the SRS score are a distillation of the Symptom Checklist items which had been reported to be more prevalent in subjects receiving anesthesia than in control subjects. The SRS items covered how the child felt generally, how the child's head, throat, and stomach felt, and how tired and weak the child felt. After the examiner read an item, the subject was asked to point to one of four pictures as the one most consistent with the way he/she felt. For example, one item is "Point to the picture which shows how your head feels." Four faces were then presented, ranging from a grimacing "lousy" to a smiling "great". Given that the SRS was an unvalidated measure and that there was some question about the ability of young children to accurately give self-reports of their experiences, the parents of children in the anesthesia group were enlisted to rate their child's behavior at each test period on four-point scales of anxiety, cooperativeness and distractibility. Each of these items was created for the present study.

TABLE 1. Measures of Intellectual and Adaptive Performance

Measure	Abilities Tapped
Information[8]	Recall of previously learned verbal information
Similarities[8]	Verbal ability
Digit span[8]	Concentration and short-term memory
Name writing[9]	Perceptual-motor speed on a well-learned task (dominant and nondominant hands)
Matching pictures[9]	
a) Errors	Abstraction ability and reasoning
b) Time	Quickness of abstraction and reasoning
Progressive figures[9]	Abstraction ability, quickness and flexibility of thinking
Selective reminding*[10,11]	
a) Recall/trial	General memory functioning, including both short- and long-term memory processes
b) Long-term storage (LTS)	Ability to enter new information into long-term storage
c) Retrieval	Efficiency of recall from long-term storage
d) Consistent long-term retrieval (CLTR)	List learning
e) Delay recall	Extended long-term recall

* Three eight-word lists were developed and were counterbalanced across the three test periods. A maximum of six trials was allowed for the child to reach the criterion of two successive complete recalls of the eight-word list. On each submeasure, higher scores indicate higher performance.

Method of Analysis

Initial comparisons of the anesthesia and control groups were carried out on each of the performance measures at Trial 1 using one-way analysis of variance. To control for resultant Trial 1 group differences, the anesthesia and control groups were then compared on each performance measure at Trial 2 using one-way

analysis of covariance, with Trial 1 scores on each measure serving as the covariate factor. Trial 3 anesthesia-control comparisons were performed similarly, with Trial 1 scores again included as a covariate factor in each one-way analysis of variance. Since only about half of the anesthesia and control subjects were tested at Trial 3, analyses were carried out to examine whether those subjects tested over three trials were representative of the subjects in their groups. Within both the anesthesia and control groups individually, the two-trial and three-trial subjects were compared on each performance measure at Trial 2 by analysis of covariance, with each subject's Trial 1 performance on a measure as the covariate factor.

Because the parent ratings of anxiety, cooperativeness and distractibility were obtained only for the anesthesia group, between-trial contrasts on each of the three items were obtained for the anesthesia group using t tests for paired samples. Responses to the Symptom Rating Scale (SRS) were compared between the anesthesia and control groups at each trial by one-way analysis of variance. Then, to examine whether group differences in symptomatology (as reflected in SRS scores) might account for differences in test performance, data from the performance measures were reanalyzed with symptomatology scores as an additional covariate factor. The added covariate in each of the Trial 2 and the Trial 3 analyses was the difference between the subject's SRS score at that trial relative to their Trial 1 SRS score.

Results

Initial comparisons of the anesthesia and control groups revealed a general tendency for the anesthesia group to perform somewhat less well than the control group across the range of performance measures at Trial 1, although the between-group differences achieved statistical significance only on three submeasures of the Selective Reminding Test. Group mean scores at Trial 1 and Trial 2 are shown in table 2, together with the results of the Trial 2 analyses of covariance which sta-

TABLE 2. Means ± SD for Anesthesia and Control Groups for Trials 1 and 2; F-score Results of Group Comparisons at Trial 2 by Analysis of Covariance, with Trial 1 Scores as the Covariate Factor

Variable	Group	Trial 1	Trial 2	F (1, 64)
Information	Anesthesia	7.28 ± 3.19	7.36 ± 3.25	2.00
	Control	7.73 ± 3.24	8.07 ± 3.49	
Similarities	Anesthesia	5.56 ± 3.76	5.75 ± 3.84	3.35
	Control	6.23 ± 3.46	6.90 ± 3.49	
Digit span	Anesthesia	6.47 ± 2.46	6.50 ± 2.67	0.18
	Control	6.87 ± 2.37	7.00 ± 2.42	
Name writing: dominant hand*	Anesthesia	2.71 ± 1.59	3.19 ± 2.24	10.22¶¶
	Control	2.68 ± 2.31	2.37 ± 1.73	
nondominant hand	Anesthesia	4.12 ± 1.84	4.27 ± 2.04	9.48¶¶
	Control	4.23 ± 2.89	3.45 ± 1.91	
Matching pictures: time†	Anesthesia	82.85 ± 28.36	63.45 ± 22.96	11.10***
	Control	82.57 ± 32.43	52.53 ± 21.65	
errors	Anesthesia	3.52 ± 2.97	2.94 ± 2.51	1.18
	Control	2.96 ± 2.58	3.10 ± 2.64	
Progressive figures‡	Anesthesia	1.07 ± 0.43	0.89 ± 0.50	4.27‡‡
	Control	0.91 ± 0.44	0.62 ± 0.37	
Selective reminding: Recall/trial§	Anesthesia	5.34 ± 1.38	4.81 ± 1.46	14.65***
	Control	6.05 ± 0.81	6.16 ± 0.76	
LTS¶	Anesthesia	29.78 ± 11.54	23.61 ± 13.22	7.37§§
	Control	34.50 ± 7.83	33.17 ± 8.66	
Retrieval**	Anesthesia	89.79 ± 10.77	85.46 ± 14.14	6.60‡‡
	Control	93.12 ± 7.26	93.99 ± 6.89	
CLTR	Anesthesia	19.39 ± 13.24	15.89 ± 13.25	5.43‡‡
	Control	27.43 ± 11.22	26.70 ± 10.76	
Delay recall††	Anesthesia	5.06 ± 2.49	3.97 ± 2.46	7.90§§
	Control	6.45 ± 1.35	6.14 ± 1.66	

* Amount of time to write the name/number of letters: Time/letter.
† Total time needed to complete the test items, in seconds.
‡ Score is log(time needed to complete the test/8).
§ Average number of words recalled per trial of the test.
¶ Total number of words scored as in long-term storage over the six trials.
** The percentage of items recalled from long-term storage.
†† The number of words recalled about 15 min after the last trial.
‡‡ $P < 0.05$; §§ $P < 0.01$; ¶¶ $P < 0.005$; *** $P < 0.001$.

tistically controlled for the initial group differences at Trial 1.

The anesthesia group's performance was significantly impaired relative to the control group on nine of the 13 measures at Trial 2. Trial 3 comparisons, also controlling for initial group differences, revealed no significant group differences across the range of performance measures. Subjects tested at Trial 3 appeared to be a representative subsample of subjects in their respective groups, for comparison of performance at the first two trials yielded no significant differences between subjects tested over two trials relative to those tested over three trials.

Results on the Symptom Rating Scale (SRS) are displayed in table 3. The anesthesia group reported a greater amount of symptomatology relative to controls at both Trial 1 and at Trial 2. Group differences were no longer present at Trial 3 the following day. Examination of the individual SRS subscales indicate that the anesthesia group's preoperative complaints were with regard to how they felt generally and how their stomachs felt. This might be accounted for by mild presurgical nervousness or by the anesthesia group having to miss breakfast in preparation for surgery. The general mildness of the complaints is indicated by the group means of the anesthesia subjects on the "stomach" and "general" items (2.68 and 3.44, respectively), referenced by "2" being "not so good", "3" being "OK" and "4" being "great". Postoperatively, at Trial 2 the anesthesia group reported feeling generally less well, with greater discomfort of the head, throat, and stomach, and of being more tired, all relative to the control group. Despite significant group differences on each of those items, the anesthesia group means were on each item toward the less symptomatic end of the scales, apparently indicating fairly mild levels of discomfort. At Trial 3 there were no significant differences on any of the SRS items.

To examine the extent to which group differences in symptomatology (as reflected in SRS scores) might account for differences in test performance, data from the performance measures were reanalyzed with symptomatology scores as an additional covariate factor. When the variance associated with symptom scores was removed, there was little change in anesthesia-control differences across the various performance measures at both Trials 2 and 3. Of the nine measures significantly impaired at Trial 2 in the previous analyses (table 2), seven

TABLE 3. Comparison of the Anesthesia and Control Groups (Means ± SD) on the Symptom Rating Scale (SRS)* by Analysis of Variance

Variable	Anesthesia	Control	F†	P
SRS				
Trial 1	18.62 ± 2.93	20.45 ± 2.73	6.49	0.013‡
Trial 2	17.79 ± 3.55	21.37 ± 2.53	21.00	0.000**
Trial 3	21.43 ± 2.59	21.67 ± 1.91	0.08	0.780
SRS subscales				
General				
Trial 1	3.44 ± 0.82	3.79 ± 0.41	4.36	0.041‡
Trial 2	3.18 ± 0.97	3.67 ± 0.55	5.99	0.017‡
Trial 3	3.64 ± 0.63	3.87 ± 0.36	1.41	0.246
Throat				
Trial 1	2.73 ± 0.96	3.17 ± 1.03	3.00	0.088
Trial 2	2.59 ± 1.13	3.60 ± 0.56	19.67	0.000**
Trial 3	3.29 ± 0.91	3.33 ± 0.72	0.02	0.877
Head				
Trial 1	3.03 ± 1.03	3.31 ± 0.89	1.32	0.256
Trial 2	2.88 ± 1.04	3.47 ± 0.73	6.62	0.013‡
Trial 3	3.71 ± 0.61	3.27 ± 0.80	2.84	0.103
Stomach				
Trial 1	2.68 ± 1.03	3.34 ± 0.86	7.62	0.008§
Trial 2	2.79 ± 0.95	3.37 ± 0.96	5.73	0.020‡
Trial 3	3.36 ± 0.93	3.47 ± 0.64	0.14	0.713
Tiredness				
Trial 1	3.26 ± 0.99	3.45 ± 0.91	0.58	0.451¶
Trial 2	2.97 ± 1.11	3.63 ± 0.61	8.36	0.005
Trial 3	3.57 ± 0.65	3.93 ± 0.26	4.03	0.055
Strength				
Trial 1	3.47 ± 0.79	3.52 ± 0.57	0.07	0.792
Trial 2	3.38 ± 0.85	3.63 ± 0.49	2.01	0.162
Trial 3	3.86 ± 0.36	3.80 ± 0.41	0.16	0.700

* On each variable, lower scores reflect greater symptomatology.
† Degrees of freedom are (1, 62) at Trials 1 and 2 and (1, 27) at Trial 3.
‡ $P < 0.05$; § $P < 0.01$; ¶ $P < 0.005$; ** $P < 0.001$.

still achieved statistical significance after covarying out the SRS effect while the two others approached significance ($P < 0.10$ on both Progressive Figures and Selective Reminding CLTR). There were again no significant group differences at Trial 3.

Parents of children in the anesthesia group rated their children as significantly more anxious at Trial 1 than at Trial 2 postsurgery ($t = 2.79$, $P < 0.01$). Still, the anesthesia group mean at Trial 1 (1.79, with "1" being "fairly calm" and "2" being "mildly anxious") indicates that parents in general saw their children as being only mildly anxious at that time. The parents' judgments of the cooperativeness and distractibility of the children did not vary significantly across the trials and in all cases the group means were toward the end of the rating scales reflecting more optimal behavior. For example, with higher scores indicating more symptomatology, mean scores on parent ratings of cooperativeness across the trials were 1.96, 2.11, and 1.84, respectively, ("2" being "about as cooperative as usual") and mean ratings of distractibility were 1.48, 1.60, and 1.31, respectively ("1" being "about as distractible as usual" and "2" being "mildly more distractible than usual").

In order to assess whether the induction methods used in the present study had a differential effect on later psychological functioning, those subjects receiving thiamylal induction were compared on Trial 2 performance with those subjects whose induction did not involve additional agents. As in previous analyses, Trial 1 scores were used as a covariate factor within an analysis of covariance. The two induction groups differed significantly on only one of the 13 measures, and there was no consistent tendency for one group to outperform the other.

Discussion

There was a clear tendency for five- to eight-year-old children receiving halothane-N_2O general anesthesia to perform at subpar levels across a range of psychological performance measures at the time of hospital discharge. There was no evidence for any continued impairment of psychological functioning the next day, approximately 24 h after exposure to the anesthesia.

With regard to the kinds of deficits measured approximately two hours after halothane-N_2O general anesthesia, there was a slowing of performance on all tasks with a time component as well as impairment of some aspects of memory functioning. The slowing of performance appeared to be quite generalized, affecting higher level abstraction ability as well as the performance of a very familiar, highly practiced perceptual-motor task, such as name writing. Within the area of memory functioning, the anesthesia did not affect short-term memory, as measured by Digit Span (repeating back a series of numbers immediately after presentation). Short-term memory refers to a very brief memory store from which information is either lost—generally within about 15 s—or transferred to long-term memory store.[12] There was considerable evidence from the Selective Reminding task that long-term memory processes were affected by the general anesthesia. The pattern of findings is not unusual, as Drummond[13] concluded in a review paper that long-term memory processes may be more sensitive to the adverse effects of anesthesia than short-term memory processes. Relative to the control group in the present study, the anesthesia group was as capable of repeating information back immediately after its presentation, but they were less capable of storing information for later recall. In addition to storing less new information in long-term memory, they were also less efficient and more inconsistent in the retrieval of that information which did get stored in long-term memory.

In addition to the performance decrement at the time of hospital discharge, the anesthesia group also reported more symptomatology on the SRS at that time. This finding raises the question: Are the deficits found a direct result of anesthetic effects on brain physiology or might lowered performance be accounted for by physical or behavioral symptoms associated with the anesthesia or surgery which result in the subject being distracted from the tasks? The vast majority of previous studies have not addressed this question, and those which have reported conflicting findings.[2,§] The SRS in the present study was derived from previous research with adults[2] and was thus not validated on children. The pattern of greater symptomatology on the SRS in the anesthesia group prior to and especially soon after surgery, combined with no difference between groups on the SRS 24 h later, lends some indication that the SRS was measuring what was intended. In general, when the variance accounted for by the symptom measure was covaried out at the different test periods, group performance differences still remained. This suggests that distraction due to physical symptoms or discomfort cannot account for the anesthesia-control differences in psychological test performance at the time of hospital discharge. This conclusion is further supported by results on the parent ratings. The parents, in general, did not see their children as being any less cooperative or any more distractible at the discharge testing than at the presurgical testing. The parents did rate their children as more anxious prior to surgery, but that would favor a relative improvement in performance at later test periods. Still further evidence that the children were not distracted and were attending to the

§ Steinhelber J, Eger EI, Durandetto BE, et al: Psychological effects of halothane and enflurane anesthesia in older patients. Abstracts of Scientific Papers, annual meeting of the American Society of Anesthesiologists, Chicago, 231–232, 1975.

tasks is the anesthesia group's stable performance on Digit Span across the test trials. Digit Span performance demands attention and concentration and is thus highly vulnerable to distraction. While these results are not conclusive, they suggest that the effects found at the time of hospital discharge may be attributed to the anesthesia and its effect on the child's brain functioning.

While halothane is most commonly delivered to the patient in mixture with nitrous oxide and oxygen, as in the present study, there is likely to be some variability between settings in the use of drugs for preparation of the patient and the induction of anesthesia. In the present study, a proportion of the anesthesia subjects had anesthesia induction with thiamylal, an ultrashort-acting barbiturate. When those subjects receiving thiamylal induction were compared on Trial 2 performance with those subjects whose induction did not involve additional agents, there was little difference between the groups and there was no consistent tendency for one group to outperform the other.

A conclusion that the halothane-N_2O mixture accounts for the performance deficits at the time of hospital discharge requires that the halothane-N_2O anesthesia did not vary with the method of induction. Since thiamylal was administered in concentration sufficient only to cause basal narcosis, the amount of halothane-N_2O required for maintenance of anesthesia was not considered to be different as a function of induction method. The data from this study thus offer suggestive evidence that thiamylal used to induce anesthesia does not compound the psychological effects of brief duration halothane-N_2O anesthesia at two hours postanesthesia. However, given that no previous studies of the psychological effects of thiamylal have been published and there are few reports regarding such effects for other barbiturates,[3] further research is recommended.

Despite the impairment of performance at the time of hospital discharge in the present study, the deficits are not sufficient to argue that the children should remain in the hospital for a longer period of time, especially given that the children are released under the care and supervision of their parents. Still, parents can expect that their children may be somewhat slower at the things they do attempt after leaving the hospital and that they may be more forgetful of any new instructions and information given. Within 24 h, however, the data suggests that the children will be functioning normally again. At that time, the child should be intellectually capable of learning and of benefiting from attendance at school. This recovery time—between two and 24 h—is comparable to what is reported for adult subjects experiencing short-duration halothane anesthesia.[5,14] The pattern of psychological impairment demonstrated in the present study also appears comparable to that found in adults following general anesthesia, with the data indicating some impairment across a range of intellectual and adaptive functions rather than discrete, specific deficits.[2,14] The results are encouraging in their suggestion that five- to eight-year-old children do not show long-term persistent deficits following brief halothane-N_2O general anesthesia. Caution is still warranted, however, in extrapolating to other age groups of children or to those receiving different lengths or types of anesthetic agents. The present study is an initial step in examining anesthetic effects in children and further research testing the general application of the findings is called for.

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