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Implicit Memory for Words Played during Isoflurane- or Propofol-based Anesthesia

The Lexical Decision Task

Sinikka Münte, M.D.,* Maren Schmidt, M.D.,* Maren Meyer, M.D.,† Wido Nager, M.D.,‡ Ekkehard Lüllwitz, M.D.,* Thomas F. Münte, M.D.,§ Siegfried Piepenbrock, M.D.‖

Background: **Unconscious processing of words during general anesthesia has been suggested after surgery with several tests of implicit memory. Patients can neither recall those words nor do they have explicit memories of other intraoperative events. It is unclear to what degree information is processed during general anesthesia and which tests are best suited to detect implicit memory. In the current study, a lexical decision paradigm not previously used to demonstrate implicit memory during anesthesia was used.**

Methods: **Sixty patients undergoing lumbar disc surgery were assigned to receive isoflurane infusion– or propofol infusion–based anesthesia combined with alfentanil infusions and a nitrous oxide–oxygen mixture. A control group of 10 medical students listened to tapes without receiving anesthesia. Two tapes, each containing a list of 30 low-frequency German nouns repeated for 15 min, were prepared, with half of the patients listening to tape A and the other half listening to tape B during the operation. Exposure time was 15 min from the time of skin incision onward. In the test phase, approximately 7 h later, words from lists A and B plus 60 nonwords were presented in random order by a computer program. Subjects were asked to indicate, by pressing one of two response buttons, whether the spoken word was or was not a legal German word (lexical decision).**

Results: **A recognition test revealed chance recognition for words presented during anesthesia. Lexical decision responses, however, were slightly faster to primed (previously presented) words than to unprimed (not previously presented) words when the entire group of patients was tested, suggesting a small implicit memory effect, which barely failed to reach the significance level. When the two medication groups were tested separately, no significant implicit memory effect could be ascertained statistically. The effects of previous exposure were much more pronounced in the control group.**

Conclusions: **Balanced anesthesia techniques with isoflurane or propofol lead to only a minimal, statistically borderline implicit memory effect in the lexical decision paradigm.**

CURRENT research suggests that on some occasions, words or phrases presented during general anesthesia can be perceived and retained in memory, even if patients cannot recall any intraoperative events.[1] Although direct tests of memory, such as free recall or recognition, do not reveal explicit memory for the presented material, certain indirect tests may reveal implicit memory.[2] Consider, for example, the stem completion task: During anesthesia, patients are presented with words. After surgery, subjects are given three-letter word beginnings (*e.g.*, BUT-) and are asked to complete them with the first word that comes to mind; no reference is made to a previous study episode. Implicit memory is indicated when patients complete a stem more frequently with a word that was presented during anesthesia (*e.g.*, BUTTON) than is expected by comparison with baseline completion rates. This facilitation of task performance under such circumstances is known as priming. Many indirect tests of memory are based on such priming effects, which are attributable to implicit memory.[3] Neuroanatomically and functionally distinct explicit and implicit memory systems have been shown in amnesic and normal subjects using neuropsychologic tests and neuroimaging procedures.[4,5] Anesthesia seems to produce—at least in some circumstances—a memory impairment similar to amnesic syndromes: explicit memory for the study material is impaired; that is, the person does not recognize the previously presented words or phrases, although implicit memory of the material may be preserved. Therefore, memory paradigms used in persons with amnesia and in healthy controls can serve as a starting point for studies of anesthetized patients.

However, implicit memory research in anesthetized patients has yielded conflicting results because approximately half of the studies report positive findings and the other half report negative findings.[6] Methodologic issues, such as lack of standardization of the study variables and varying study designs, may be responsible for the inconsistency. Besides, many factors may influence the retention of implicit memory, including the anesthetics and their dosages, the intensity of surgical stimuli, the nature of the test material, the modality in which stimuli are presented during study and test phases (auditory–visual *vs.* auditory–auditory), the length of the study test interval, and the physiologic status of the patients.[7]

Therefore, it is currently unclear which kind of information patients continue to process and store during general anesthesia and what measures are best suited to detect implicit memory for such information. Previous research has suggested that implicit memory can be demonstrated most readily for simple auditory stimuli,

* Staff Anaesthesiologist, ‖ Professor, Department of Anaesthesiology, ‡ Resident, Department of Neurology, † Medical Student, Medical School of Hanover. § Professor, Department of Neuropsychology, University of Magdeburg, Magdeburg, Germany.

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Address reprint requests to Dr. Münte: Department of Anaesthesiology, Medical School of Hanover, Carl-Neuberg-Strasse 1, 30625 Hanover, Germany. Address electronic mail to: Muente.Sinikka@ MH-Hannover.de. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

Table 1. Patients: Anesthetic and Surgical Details

	Isoflurane	Propofol
Age (yr)*	35.9 ± 6.5	34.7 ± 6.1
Weight (kg)*	78.7 ± 14.1	79.2 ± 9.9
Height (cm)*	179.4 ± 9.9	174.7 ± 8.8
Women/men†	12/18	11/19
Education (yr)*	10.4 ± 1.6	10.3 ± 1.6
Employed/unemployed/student (No.)†	25/4/1	28/2
ASA I/ASA II†	21/9	19/11
Duration of anesthesia (min)*	126.3 ± 40.0	119.0 ± 27.4
Duration of surgery (min)*	78.2 ± 34.7	71.2 ± 19.9
Total dose of propofol (mg)	246.3 ± 62.0	1,188.5 ± 347.1
Boluses of extra propofol (mg)	1 × 100, 1 × 80, 1 × 50	
Total dose of alfentanil (mg)*	4.49 ± 1.93	4.10 ± 0.83
End expiratory concentration of isoflurane (%)/ blood concentration of propofol (μg/ml)	1.06 ± 0.35	3.31 ± 0.42
Blood concentration of alfentanil (ng/ml)‡	85.54 ± 5.72	85.54 ± 5.72
Postoperative piritramid until testing (mg)§	8.55 ± 5.33	13.38 ± 6.27

Values are mean ± SD.

* Nonsignificant, Mann–Whitney U test. † Nonsignificant, chi-square test. ‡ The blood concentrations of alfentanil were simulated postoperatively with StanPump software. StanPump is freely available from the author, Steven L. Shafer, M.D., Anesthesiology Service (112A), PAVAMC, 3801 Miranda Avenue, Palo Alto, California 94304. § $P < 0.01$, Mann–Whitney U test.

ASA = American Society of Anesthesiologists (physical status).

such as single, relatively familiar words, although a recent study from our own group showed that even complex material (stories) was processed during propofol–alfentanil–nitrous oxide anesthesia.[8] This effect was not replicated in a subsequent study using isoflurane under similar conditions.[9]

Our primary goal in the current study was to adapt a new task of implicit memory, the lexical decision task, for use in anesthetized patients. Although commonly used in studies in amnesic and normal subjects, it has not previously been used during anesthesia conditions.[10–15] Further, we wished to confirm the finding that implicit memory performance can be influenced differently by the two anesthetics. Therefore, we used a similar study design as in the previous studies, including the same study test interval, surgical procedure (removal of lumbar disk), and inclusion and exclusion criteria for the study populations. A healthy, nonanesthetized control group was tested using the same study test procedures to demonstrate that the paradigm can be used to demonstrate implicit memory.

Materials and Methods

Patients

With approval from the local institutional review board (Medical School of Hanover, Hanover, Germany) and written informed consent of each participant, 64 patients undergoing lumbar disk surgery and 10 controls without anesthesia were enrolled in the study between December 1998 and April 2000 (table 1). The data from four patients were excluded from the results because the data were not correctly saved[3] or the patient refused to participate in postoperative testing.[1] Therefore, the results are based on 30 patients in the isoflurane group (isoflurane was the main anesthetic agent), 30 patients in the propofol group (propofol was the main anesthetic agent), and 10 controls. On the day before surgery, the patients were informed that an audio tape with word lists would be played to them during the operation and that they would undergo a short interview and a psychologic test several hours after the operation. Patients older than 45 and with a native language other than German were excluded, as were those with neurologic diseases, memory dysfunction, psychiatric diseases, head trauma, hearing impairment, or psychoactive medication. A control group consisted of 10 volunteer medical students who listened to the tapes without anesthesia and completed the implicit and explicit memory tests after a comparable delay.

Sample Size Estimations

Two questions were asked by the current study[1]: is there a priming effect for material presented during anesthesia using the lexical decision task?[2] and is there a difference between isoflurane- and propofol-based anesthesia techniques? For the first question, each group (anesthesia technique) could be viewed as an independent study with a within group comparison of two means (primed and unprimed words). Repetition priming studies the lexical decision task have yielded a size of the priming effect between 50 and 100 ms with reaction times of approximately 600 ms (SD 80 ms).[16] Based on these data, the sample size was calculated as 18 (power 80%).#

de Leeuw J: Power Calculator. Available at: http://ebook.stat.ucla.edu/calculators/powercalc/normal/n-1/n-1-samp.htrml. Accessed August 29, 2001.

For the second question, sample size estimation was based on an anticipated SD of the size of the priming effect of 50 ms and a difference of the priming effect between the two groups of 40 ms. This was done because smaller differences in priming effects between the two anesthetic regimens would not have been of clinical interest. This yielded an estimated sample size of 26 (power of 80%, $\alpha = 5\%$).[17]

Anesthesia

Anesthesia was administered by two of the authors (M. S. and E. L.). Patients were randomly assigned to one of two anesthetic regimens: isoflurane–alfentanil–nitrous oxide or propofol–alfentanil–nitrous oxide. All patients were premedicated with 7.5 mg oral midazolam 0.5–1 h before anesthesia.

Isoflurane–Alfentanil–Nitrous Oxide Anesthesia. After administration of 0.5 mg intravenous atropine, anesthesia was induced with 2–2.5 mg/kg propofol and 10 $\mu g \cdot kg^{-1} \cdot h^{-1}$ alfentanil. After the patients lost consciousness, they underwent ventilation with 100% oxygen, and 0.5 mg/kg atracurium was administered to facilitate tracheal intubation. Immediately after induction, an alfentanil infusion of 30 $\mu g \cdot kg^{-1} \cdot h^{-1}$ was started, and isoflurane up to 1.5% was added to oxygen. Anesthesia was maintained with isoflurane at an end-expiratory concentration of 1.06 $\pm$ 0.3% combined with 60% nitrous oxide. The inhaled anesthetics and alfentanil infusion were kept constant until the end of surgery. Additional propofol (0.5–1 mg/kg) was administered whenever heart rate or arterial blood pressure levels increased by more than 10% of preoperative values. Atracurium (5–10 mg) was administered when more than two twitches of the train-of-four were present. Electric activity of the heart, noninvasive blood pressure, ventilation, end expiratory concentrations of carbon dioxide and inhaled anesthetics, peripheral oxygen saturation, and neuromuscular transmission were continuously monitored.

Propofol–Alfentanil–Nitrous Oxide Anesthesia. The anesthesia technique differed from the previously described only in that instead of boluses of propofol and isoflurane, target-controlled infusion (3500 TCI Graseby; Graseby Medizintechnik GmbH, Kirchseeon, Germany) of propofol was used for induction and maintenance of anesthesia. The initial target concentration during the intubation was 10 μg/ml and was reduced to a target concentration of approximately 3.3 μg/ml during the tape presentation (table 1).

Study and Test Procedures

Presentation of Auditory Stimuli. Two audio tapes, each consisting of a list of 30 different low-frequency German nouns (all $<$ 50 occurrences per 1,000,000, mean frequency 8.9/1,000,000, frequency matched between lists)[18] were prepared. One half of the participants from each group (15 each from the isoflurane and propofol groups and 5 from the control group) were exposed to the first list during the study phase, and the other half listened to the second tape. Presentation was started at the time of skin incision. The same format was used for each control participant without anesthesia. The words were repeated in varying sequences 10 times during a 15-min period at a rate of one word every 3 s by a male voice. The control participants were asked to count how many times they heard a certain word to ensure that they were listening and to prevent them from rehearsing the words. The investigator (M. M.) who conducted the postanesthetic memory tests and interviews was blinded to the tape contents.

Implicit Memory Test: Lexical Decision. Implicit and explicit memory for the words and explicit memory for intraoperative events and dreams was assessed 6–8 h after exposure to the tapes. Implicit memory was tested first using a lexical decision paradigm. Subjects were asked to decide as quickly as possible whether the stimulus presented was a real word or a nonword. It has been shown numerous times that previous exposure to test stimuli speeds up this decision, leading to shorter response latencies of primed words relative to unprimed words. A practice trial using 20 items that were not included in the experimental tapes was performed before the test session.

For the test session, words from both tapes plus 60 nonwords were spoken by the same male voice that had been used for the study tapes. These words were AD converted at a rate of 22,700 Hz, digitally edited to determine word onset for trigger purposes, and stored on magnetic disks. Primed and unprimed words and nonwords were presented in random order by a special purpose computer program at an interstimulus interval of 2,700 ms (stimulus duration 500–800 ms). The participants were instructed to listen to the stimuli and to press a button held in the right hand whenever a stimulus qualified as a legal German word, and to press a button held in the left hand whenever a stimulus was not a German word. The reaction times for the different events were recorded by the computer from the onset of the stimulus to the patient's response.

Explicit Memory Tests: Recall and Word Recognition. Explicit memory for intraoperative events was assessed using a structured interview pertaining to (1) the final memories before falling asleep, (2) the initial memory on waking, and (3) to dreams or other experiences during surgery. Finally, a recognition test for the word lists was administered. Patients and control participants were given a page containing a random list of the 30 primed and the 30 nonprimed words. The participants were asked to indicate which words had been played during the test phase and how certain they were about their decision (yes–certain, yes–uncertain, no–certain, no–uncertain).

Table 2. Mean Response Latency (in Milliseconds) and Error Rates to Unprimed and Primed Words

	Isoflurane, RT (ms)	Isoflurane, Error Rate (%)	Propofol, RT (ms)	Propofol, Error Rate (%)	Controls, RT (ms)	Controls, Error Rate (%)
Unprimed words	1,021 ± 136	3.5 ± 1.8	976 ± 126	3.2 ± 1.2	861 ± 46	2.0 ± 0.9
Primed words	994 ± 97	3.1 ± 1.7	968 ± 112	3.1 ± 1.3	789.4 ± 48	1.9 ± 0.8

RT = reaction time.

Statistical Analysis

Mean reaction times for all correctly classified primed words and all unprimed words were determined for each subject separately and entered into statistical analysis. The statistical comparisons were done by analysis of variance with group (isoflurane *vs.* propofol) as a between-subjects factor and repetition (primed *vs.* unprimed words) as a within-subjects factor. Because there was concern that the postanesthetic state in the patient group might have led to an increased number of very long reaction times, therefore somewhat corrupting the utility of the individual mean reaction times, several additional analyses were conducted on (1) the median reaction times, (2) the mean reaction time after exclusion of outliers in the individual data sets using the Grubbs test,** and (3) the mean reaction time after rejection of all values exceeding 2.5 SDs over the individual mean. Finally, error rates were determined and expressed as percentages.

Results

Lexical Decision Task

The principal question was whether response latencies would be affected by previous exposure to the words. The results are presented in table 2. It can be seen that the lexical decision latencies for the control group showed faster reactions to primed words than to unprimed words (*t* test, $P < 0.0001$). Although patients of both study groups were slightly faster for the primed words, the main effect of repetition just failed to reach the significance level (analysis of variance, $F_{1,59} = 3.89$; $P = 0.0537$) when the individual subjects' means were used. *Post hoc* comparisons indicated a marginally significant effect of repetition in the isoflurane group ($P < 0.09$), whereas the effect in the propofol group was not significant ($P > 0.3$). There was no group by word type interaction ($F_{1,59} = 1.03$). Faster reaction times for primed words were found in 22 of 30 patients of the isoflurane group, 18 of 30 patients of the propofol group, and in all 10 control subjects.

For the analyses on the medians and means (with outliers removed), the results were similar in that the effect of repetition was marginally significant (median $F_{1,59} = 3.61$; $P = 0.062$; outlier removed $F_{1,59} = 4.05$; $P = 0.048$††). For the analysis on the means (after rejection of all values above the 2.5-SD limit, table 3), the effect of repetition was significant ($F_{1,59} = 4.66$; $P = 0.035$). No group by word type interaction was present for this measure ($F_{1,59} = 1.33$). Again, *post hoc* tests indicated a marginally significant effect of repetition in the isoflurane ($P < 0.06$) but not in the propofol group ($P > 0.3$). For this measure, the effect sizes[19] were 0.28 for the isoflurane group (power 0.44) and 0.07 for the propofol group (power 0.10). An analysis of variance on the errors did not reveal any significant effects of repetition or anesthetic technique (all $F_{1,59} < 1.5$).

Recall and Word Recognition

None of the participants reported conscious recollection of events during surgery. Two patients of the propofol group had had a pleasant dream that was not related to any intraoperative events. One patient reported that she had dreamt of having her wound drainage removed, which actually was a recall of an immediate postoperative event. In the word recognition test, half of each study group indicated that they were sure about not having heard any words during anesthesia. Another half indicated that they probably had heard some words. However, all subjects were at chance level with regard to the recognition decision (49.3 ± 3.9% of words were classified correctly), regardless of how sure the patients were that they had or had not heard those words. In the group of control subjects, however, the results were different, with 82.8% (SD 5.5) of the words classified correctly in the recognition test.

Because some theorists posit that recognition memory can be influenced by both explicit and implicit memory processes,[20] we examined the question of whether forced choice recognition judgments and individual priming effects were correlated. This analysis was performed for the isoflurane group only because this group showed at least a marginal priming effect. It turned out that there was no correlation between the recognition performance (at chance for the entire group) and priming (Pearson $r = -0.2026$, $P = 0.28$).

Discussion

We observed a robust reaction time effect in our nonanesthetized control group and a tendency toward

** Grubbs Test for Detecting Outliers. Available at: http://www.graphpad.com/calculators/grubbs2.cf. Accessed April 21, 2001.

†† In the propofol group, on average, 2.4 (SD 1.8) of 30 data points were removed, whereas in the isoflurane group, 2.5 (SD 1.7) of 30 data points were eliminated.

Table 3. Mean Response Latency (in Milliseconds) to Unprimed and Primed Words

	Isoflurane, RT (ms)	Propofol, RT (ms)
Unprimed words	1,005 ± 112	961 ± 118
Primed words	976 ± 91	953 ± 104

Data exceeding 2.5 SD rejected.

RT = reaction time.

quicker reaction times for intraoperatively presented words in the patients. Because the patients had no recall of the intraoperative period and the recognition of the words was at chance level, the finding should be interpreted in terms of a small effect of implicit memory. This dissociation between explicit and implicit memory after surgery and anesthesia was not observed in the awake controls, who performed above chance level in the word recognition test. The slow reaction times of the patients (compared with the controls) suggest that both patient groups experienced a general cognitive slowing due to the anesthesia. In this situation, lapses of attention might lead to lapses of attention in the trials with very long reaction times. Consequently, any priming effect, if present, might be masked. In the literature, different methods to deal with such skewed reaction time distributions have been suggested.[21] Simulation studies and studies with real data, however, have not resolved the question as to which of these methods is superior. Therefore, we conducted several additional analyses with different methods of outlier correction. All of these analyses suggested the same thing, *i.e.*, the effect of repetition (implicit memory) was significant at approximately the 5% level. The inspection of the means suggest that this main effect of repetition was mainly attributable to the isoflurane group. The group by repetition interaction, however, was not significant in any of the analyses. The effect size (Cohen d)[19] in the isoflurane group was 0.28 and thus within the same range found by Merikle and Daneman[6] in their meta-analysis of implicit priming studies and anesthesia. These authors determined that effect sizes decrease systematically as the interval between surgery and test increases. For the first 12 h after surgery, an average effect size of 0.22 was found in the meta-analysis.

The reason to adopt the lexical decision task was its principal ability to quantify even weak memory effects in terms of millisecond changes in decision times. It has been shown to be a sensitive index of implicit memory in both normal subjects and amnesic persons.[10–15] To our knowledge, it has not been previously used in anesthetized patients. Methodologic aspects, such as the type of verbal information and anesthetic aspects, which may account for the reduced memory performance in our experimental groups, are discussed in the following section.

In the current study, the lexical decision task was used in the same format as in most studies of amnesic and normal persons. The same study test modality, low-frequency words, and several repetitions of the study words during anesthesia were obtained because these factors have been shown to enhance the performance on test session. However, a review of the implicit memory studies conducted in anesthetized patients reveals that these factors may differ during anesthesia conditions. For example, the type of words used in this study may have reduced the memory effect. A robust implicit memory effect has been demonstrated with the word stem completion task if familiar words were used as stimuli.[22,23] The effect was small or no more detectable if unfamiliar words were presented intraoperatively.[24,28] The same pattern of results has been observed in studies using the category generation task.[24–27] It seems that during anesthesia conditions, a familiar and meaningful item leaves a stronger and more accessible trace in memory than a less familiar one. The results of the current study are in line with this suggestion. However, this observation in anesthetized patients contrasts sharply with the findings with healthy participants and with amnesic patients, in which priming in lexical decision is generally larger for less familiar words than for familiar words.[14]

Another feature of the implicit memory that seems to differ during anesthesia conditions is the durability of the memory trace. For example, smaller word priming effects were found if the implicit memory tests were applied the day after surgery or even later.[24,28] In studies of amnesic and normal controls, the durability of the memory trace has been shown to be better for familiar words than for unfamiliar words.[13] It is unclear whether this is the case in anesthetized patients.

A further source of discrepancy is the fact that there are less experiments in auditory modality than in visual modality in the amnesic literature, and those results may be valid only for the particular task and study conditions. In visual modality, the priming effects in the lexical decision task have been shown up to 2 days after the first stimulus presentation. However, this finding may not account for auditory modality.[29]

The results of the current study are somewhat surprising if compared to our previous results. Using a postoperative reading speed task, we found an implicit memory effect for stories presented during propofol–alfentanil–nitrous oxide anesthesia but not in a subsequent study during isoflurane–alfentanil–nitrous oxide anesthesia.[8,9] In the current study, we did not find a clear differential effect of the two anesthetic regimens on the lexical decision task. However, a stronger tendency toward an enhanced implicit memory performance was detected during isoflurane-based anesthesia. The lexical decision task, unlike the reading speed task, does not require information processing at a high cognitive level. Therefore, we predicted that using experimental conditions similar to those in the reading speed experiments, we should find a word priming effect at least in patients to whom propofol-based anesthesia was administered. Given our current results, the question arises of why the same anesthetic regimen abolished implicit memory effects in one task but not in the other. One possible explanation is that these two tasks tap different sources of implicit memory and are therefore not directly comparable. On the lexical decision task, perceptual features, such as phoneme structure, voice of the speaker, and so forth, facilitate processing on reexposure. The memory process in this type of task is called perceptual priming. The stories tested by reading speed task in our previous study required another type of memory processing, called conceptual priming. The term implies that for a reader to benefit from previous exposure to such stories, processing at a postperceptual, conceptual level is required.[30] These two levels of processing—perceptual *versus* conceptual—may affect the durability and strength of the memory trace.[13] Memory traces that include the stimulus and its context may be stronger than those of the stimulus alone.[31] For example, associations for stories presented during general anesthesia have been demonstrated 24 h to 5 days after surgery.[32,33]

The available literature suggests that single words can be processed under relatively high end-expiratory concentration (1.0 ± 0.5%) of isoflurane.[23] If surgical stimulus is lacking, lower concentrations (up to 0.8%) are sufficient to suppress implicit memory.[34] The isoflurane group of our study received an end-expiratory concentration of 1.06 (± 0.35)%. Propofol has been used less frequently in studies of implicit memory. Most of these studies, all using relatively low infusion rates, have reported positive implicit memory effects.[35–37] In our previous study, implicit memory was found under propofol concentrations of 2.78 μg/ml,‡‡[1] whereas in the current study, the concentration was 3.3 (± 0.4) μg/ml. It might be that the plasma concentrations of the current study were better controlled because individual target controlled infusions were used. These concentrations of isoflurane and propofol may attenuate the strength of the memory trace to a degree that is barely detectable by the lexical decision task. In all three experiments, patients received oral premedication of 7.5 mg midazolam, which might in addition suppress implicit memory. However, the current literature implies that midazolam, even if exercising an amnesic effect on explicit memory, has a minor effect on implicit memory.[38]

‡‡ The simulation software of StanPump was used postoperatively to determine the plasma concentrations of propofol during the stimulus tape presentation. StanPump is freely available from the author, Steve L. Shafer, M.D., Anesthesiology Service (112A), PAVAMC, 3801 Miranda Avenue, Palo Alto, California 94304.

Because many studies suggest that learning may occur in deeply anesthetized patients, we should determine which kind of implicit memory processing this might be. Because the performance in memory test depends greatly on the strength and durability of the memory trace left in memory by the first presentation, and the memory trace left during general anesthesia would presumably be weak, the indirect tests of memory used in amnesic studies need further validation and modification for anesthesia conditions.

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References

1. Ghoneim MM, Block RI: Learning and memory during general anesthesia: An update. Anesthesiology 1997; 87:387–410
2. Schacter DL: Implicit memory: History and current status. J Exp Psychol (Learn Mem Cogn) 1987; 13:501–18
3. Richardson-Klavehn A, Bjork RA: Measures of memory. Annu Rev Psychol 1988; 39:475–543
4. Shimamura AP: Priming effects in amnesia: Evidence for a dissociable memory function. Q J Exp Psychol 1986; 38A:619–44
5. Schacter DL: The cognitive neuroscience of memory: Perspectives from neuroimaging research. Philos Trans R Soc Lond B Biol Sci 1997; 352:1689–95
6. Merikle PM, Daneman M: Memory for unconsciously perceived events: Evidence from anesthetized patients. Conscious Cogn 1996; 5:525–41
7. Andrade J: Learning during anaesthesia: A review. Br J Psychol 1995; 86:479–506
8. Münte S, Kobbe I, Demertzis A, Lüllwitz E, Münte TF, Piepenbrock S, Leuwer M: Increased reading speed for stories presented during general anesthesia. Anesthesiology 1999; 90:662–9
9. Münte S, Lüllwitz E, Leuwer M, Mitzlaff B, Münte TF, Hussein S, Piepenbrock SA: No implicit memory for stories played during isoflurane/alfentanil/nitrous oxide anesthesia: A reading speed measurement. Anesth Analg 2000; 90:733–8
10. Meyer DE, Schvaneveldt RW: Facilitation in recognizing pairs of words: Evidence of a dependence between retrieval operations. J Exp Psychol 1971; 90:227–34
11. Forbach GB, Stanners RF, Hochhaus L: Repetition and practice effects in a lexical decision task. Mem Cogn 1974; 2:337–9
12. Rugg MD: The effects of semantic priming and word repetition on event-related potentials. Psychophysiology 1985; 22:642–7
13. Bentin S, Moscovitch M: The time course of repetition effects for words and unfamiliar faces. J Exp Psychol (Gen) 1988; 117:148–60
14. Verfaellie M, Cermak LS, Letourneau L, Zuffante P: Repetition effects in a lexical decision task: The role of episodic memory in the performance of alcoholic Korsakoff patients. Neuropsychologia 1991; 29:641–57
15. Bentin S, Moscovitch M, Heth I: Memory with and without awareness: Performance and electrophysiological evidence of savings. J Exp Psychol (Learn Mem Cogn) 1992; 18:1270–83
16. Münte TF, Heinze HJ: Brain potentials reveal deficits of language processing after closed head injury. Arch Neurol 1994; 51:482–93
17. Sokel RR, Rolf FJ: Biometry. New York, W H Freeman, 1981, p 263
18. Baayen RH, Piepenbrock R, van Fijn H: The Celex Lexical Database (CD-ROM). Linguistic Data Consortium, University of Pennsylvania, Philadelphia, 1993
19. Cohen, J: Statistical Power Analysis for the Behavioral Sciences, 2nd edition. Hillsdale, NJ, Erlbaum,1988
20. Jacoby LL, Dallas M: On the relationship between autobiographical memory and perceptual learning. J Exp Psychol Gen 1981; 110:306–40
21. Ratcliff R: Methods for dealing with reaction time outliers. Psychol Bull 1993; 114:510–32
22. Bonebakker AE, Bonke B, Klein J, Wolters G, Stijnen T, Passchier J, Merikle PM: Information processing during general anesthesia: Evidence for unconscious memory. Mem Cogn 1996; 24:766–76
23. Lubke GH, Kerssens C, Phaf H, Sebel PS: Dependence of explicit and implicit memory on hypnotic state in trauma patients. Anesthesiology 1999; 90:670–80
24. Block RI, Ghoneim MM, Sum Ping ST, Ali MA: Human learning during general anaesthesia and surgery. Br J Anaesth 1991; 66:170–8

25. Roorda-Hrdlickova V, Wolters G, Bonke B, Phaf RH: Unconscious perception during general anaesthesia, demonstrated by an implicit memory task, Memory and Awareness in Anaesthesia. Edited by Bonke B, Fitch W, Millar K. Amsterdam, Swets & Zeitlinger, 1990, pp 150–5

26. Jelicic M, Bonke B, Appelboom DK: Indirect memory for words presented during anaesthesia (letter). Lancet 1990; 336:249

27. Bonebakker AE, Bonke B, Klein J, Wolters G, Hop WCJ: Implicit memory during balanced anaesthesia: Lack of evidence. Anaesthesia 1993; 48:657–60

28. Hughdahl K, Mathiesen JR, Gullestad S: Implicit memory during anaesthesia: Attempt at replication. Int J Neurosci 1996; 87:63–9

29. Scarborough DL, Cortese C, Scarborough HS: Frequency and repetition effects in lexical memory. J Exp Psychol Hum Percept Perform 1977; 3:1–17

30. Tulving E, Schacter DL: Priming and human memory systems. Science 1990; 247:301–6

31. Jacoby LL: Perceptual enhancement: Persistent effects of an experience. J Exp Psychol (Learn Mem Cogn) 1983; 9:21–38

32. van der Laan WH, van Leeuwen BL, Sebel PS, Winograd E, Baumann P, Bonke B: Therapeutic suggestions has no effect on postoperative morphine requirements. Anesth Analg 1996; 82:148–52

33. Schwender D, Kaiser A, Klasing S, Peter K, Pöppel E: Midlatency auditory evoked potentials and explicit and implicit memory in patients undergoing cardiac surgery. ANESTHESIOLOGY 1994; 80:493–501

34. Andrade J, Munglani R, Jones JG, Baddeley AD: Cognitive performance during anesthesia. Conscious Cogn 1994; 3:148–65

35. Sarasin DS, Ghoneim MM, Block RI: Effects of sedation with midazolam or propofol on cognition and psychomotor functions. J Oral Maxillofac Surg 1996; 54:1187–93

36. Polster MR, Gray PA, O'Sullivan G, McCarthy RA, Park GR: Comparison of the sedative and amnesic effects of midazolam and propofol. Br J Anaesth 1993; 70:612–6

37. Bethune DW, Ghosh S, Gray B, Kerr L, Walker IA, Doolan LA, Harwood RJ, Sharples LD: Learning during general anaesthesia: Implicit recall after methohexitone or propofol infusion. Br J Anaesth 1992; 69:197–9

38. Hirshman E, Passannante A, Henzler A: The effect of midazolam on implicit memory. Brain Cogn 1999; 41:351–64