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Memory Formation during General Anesthesia for Emergency Cesarean Sections

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Background: **Occurrence of explicit memory (*i.e.*, conscious recall) has been reported especially after surgical procedures in which anesthesia is considered to be "light." In addition, previous research has shown that implicit memory (*e.g.*, improved memory test performance in absence of conscious recall) decreases with increasing hypnotic state. The current study investigated explicit and implicit memory during emergency cesarean sections with consistently light levels of hypnotic state.**

Method: **Words were presented *via* headphones, and the bispectral index was recorded throughout surgery. Memory for the presented words was tested after recovery with a word-stem completion test. Using both parts of the process dissociation procedure allowed separation of explicit and implicit memory. In the "inclusion" part of the process dissociation procedure, patients are asked to complete word stems, if possible, with the corresponding words recalled from the intraoperative presentation. In the "exclusion" part, patients are instructed to avoid the words presented intraoperatively and to use other words instead. In the absence of recall, patients are asked to use the first word that comes to mind.**

Results: **The mean bispectral index during word presentation was 76.3 (±3.0). On average, the 24 patients were able to make correct inclusion–exclusion decisions: In the inclusion part, hit rates (*i.e.*, the probability of responding with a word presented during surgery) were higher than base rates (0.37 *vs.* 0.31), whereas in the exclusion part hit rates were lower (0.23 *vs.* 0.28). Importantly, the patients made these inclusion–exclusion decisions without being able to consciously recall the words presented during surgery.**

Conclusions: **This study shows that if words are presented at relatively light levels of anesthesia, patients are able to control their inclusion–exclusion decisions. This weak form of explicit memory can occur in the absence of conscious recall. (Key words: Controlled memory; uncontrolled memory; depth of anesthesia.)**

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MEMORY of intraoperative events has been reported, especially after surgical procedures in which general anesthesia is considered to be "light."[1-3] Emergency cesarean sections during general anesthesia belong to that category, and evidence of explicit memory (*i.e.*, conscious recall) has been shown.[4,5] Two features that often are uncontrolled in studies of memory function during anesthesia are the adequacy of hypnosis and the type of memory (explicit *vs.* implicit) being studied.[5,6] In the current study, the electroencephalogram-based bispectral index (BIS) was used as a measure of hypnotic state.[7-9] Because so-called implicit memory tests do not necessarily measure implicit memory exclusively, but might be confounded by explicit memory, it is necessary to clearly separate both types of memory.[10] One method to obtain this separation is by means of the process dissociation procedure (PDP).[11-13] The PDP consists of two parts, an inclusion and an exclusion part, and can be used in combination with a word-stem completion test. Suppose the word "fancy" has been presented to a patient during surgery. Explicit memory would be evident if the patient recalls the presented word. In that case, the patient is able to complete the word stem "fan" with the word "fancy" if asked to do so (inclusion test), or to use a different word (*e.g.*, "fantastic") if instructed not to use

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the presented word for completion (exclusion test). Conversely, implicit memory would, in both parts of the test, result in a higher proportion of completion with the word "fancy" if that word had been presented *via* headphones during surgery than if it had not been played. Combining both parts of the PDP allows us to quantify the proportions of explicit and implicit memory. It is shown here that the division into explicit and implicit memory provided by the PDP is too crude to describe adequately the underlying processes and needs further refinement.

In a previous study that investigated memory in anesthetized patients undergoing trauma surgery, we demonstrated that the probability of implicit memory decreases with increasing hypnotic depth.[14] However, no reliable evidence was found for explicit memory, which may have resulted from the finding that, on average, patient BIS levels were considered to indicate adequate anesthesia (*i.e.*, mean BIS = 54). The current study was designed to extend our understanding of how memory functions during anesthesia by studying a group of patients (undergoing emergency cesarean section) in whom hypnotic state was anticipated to be consistently light.

Materials and Method

The study was approved by the Human Investigations Committee of Emory University School of Medicine, Atlanta, Georgia. Because of the urgent nature of emergency cesarean sections, informed consent could not be obtained in a reliable manner before surgery and was obtained before presentation of the memory test. Twenty-four consenting patients undergoing emergency cesarean sections were studied. All patients spoke English as their first language and had no known hearing problems.

The 32 five-letter words used as stimulus material in this study were the same as in the trauma anesthesia study.[14] The words were selected based on the results in a pilot study, such that, without previous presentation, word stems were completed with the selected words an average of 30% of the time (*i.e.*, base rate of completion equaled 0.3, with SD of 0.022). The 32 words were assigned randomly to four lists, two of which were presented during surgery (*i.e.*, 16 target words). The memory test consisted of all words, thus including the two lists that had not been presented (*i.e.*, 16 distractors). During testing, two lists were used in the inclusion part (one target and one distractor list); the remaining two lists were used in the exclusion part. As in the trauma study, we applied a counterbalancing schema (table 1) to use each word equally often as target and as distractor in both parts of the memory test. During surgery only two lists (*i.e.*, target words) are presented; the postoperative memory test consists of all four lists (target and distractors). For example, if a patient had been assigned randomly by the computer to group 3, she or he would have been presented lists 1 and 3 during surgery as target words and would have been tested in the inclusion part on lists 3 and 4 and in the exclusion part on lists 1 and 2.

Table 1. Counterbalancing Schema

	List 1 (Words 1–8)	List 2 (Words 9–16)	List 3 (Words 17–24)	List 4 (Words 25–32)
Group 1	Inclusion target	Inclusion distractor	Exclusion target	Exclusion distractor
Group 2	Exclusion distractor	Inclusion target	Inclusion distractor	Exclusion target
Group 3	Exclusion target	Exclusion distractor	Inclusion target	Inclusion distractor
Group 4	Inclusion distractor	Exclusion target	Exclusion distractor	Inclusion target

The standardized anesthetic procedure consisted of a rapid-sequence induction with 4 mg/kg thiopental and 100 mg succinylcholine to facilitate tracheal intubation. Before delivery, anesthesia was maintained with 50% nitrous oxide and oxygen with 0.2% isoflurane (end-tidal concentration). After delivery, the nitrous oxide concentration was increased to 70%, with 0.2% isoflurane (end-tidal) and 0.1–0.15 mg/kg morphine. No benzodiazepine or scopolamine was administered. None of the patients received exogenous central nervous system active agents in the 6 h before surgery.

The target words were played to the patients *via* closed headphones, which were connected to a Macintosh PowerBook 180 (Apple Computers, Cupertino, CA). The program for word presentation was started directly after drug concentrations were altered postdelivery. The program assigned each patient to one of four groups and presented two word lists in a random order according to the counterbalancing scheme. Each word was repeated consecutively 12 times with a 2-s delay between repetitions, resulting in an approximate 14-min duration of word presentation. BIS was recorded on a microcomputer throughout surgery using an A1000 monitor (Aspect Medical Systems, Natick, MA) with a two-channel referential montage.

Within hours after surgery, as soon as the patient was

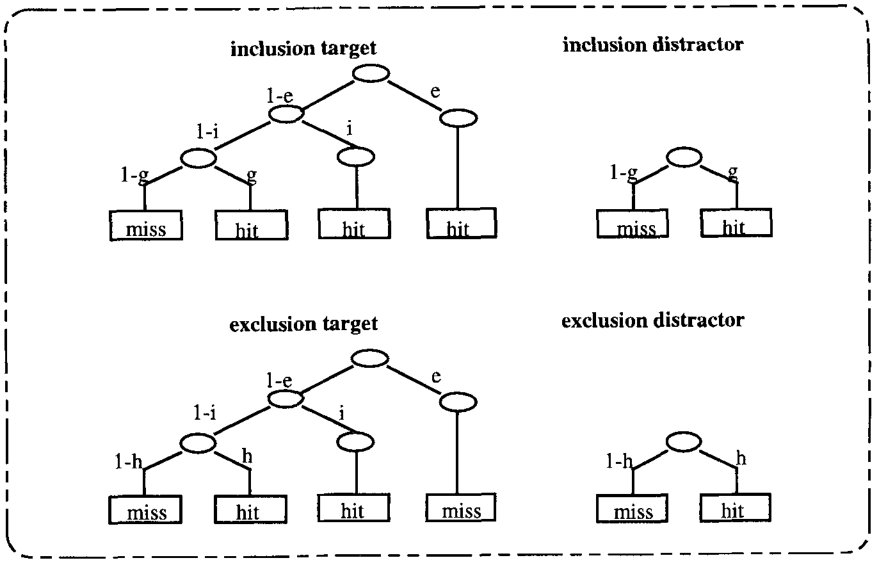

Fig. 1. The multinomial processing model of memory of Buchner *et al.*[15] The parameter *e* represents explicit memory, *i* represents implicit memory, and *g* and *h* are the base-rate parameters in the inclusion and exclusion parts, respectively.

responding adequately postoperatively, informed consent was obtained and the patient was asked about recall of pre-, intra-, and postoperative events using a short, structured interview. After a short word-stem completion exercise to familiarize the patient with the computerized test procedure, the inclusion and exclusion parts of the word-stem completion test were administered. The order of the two parts was varied among patients. Each part was introduced by a thorough explanation of the corresponding test instruction. In the inclusion part, patients were asked to try to complete the word stem, which was presented audibly and visually, with the corresponding word presented during surgery. If unable to recall the word from surgery, the patient was asked to fill in the first word that came to mind. In the exclusion part, patients were instructed to avoid the words presented during surgery and to use other words instead. As before, in case of no recall, patients were asked to fill in the first word that came to mind. The presentation of word stems was controlled by the word-stem test computer program. The responses were entered into the computer database by the observer. To assess whether patients consciously recalled the words from surgery, the patients were asked to report each recalled word during the word-stem completion test.

Statistical Analysis

Observed hit rates (*i.e.*, the probability of responding with a word presented during surgery) for targets were compared with the hit frequencies for distractors using the exact binomial test. In case of implicit memory, higher hit rates would occur in both parts of the test. In the case of explicit memory we would expect a higher hit rate in the inclusion part, combined with a hit rate lower than the base rate in the exclusion part. Absence of memory is indicated by base-rate performance in both parts of the test.

Using the Buchner *et al.* multinomial processing model of memory (fig. 2), the observed hit frequencies for targets and distractors in the inclusion and exclusion parts of the stem completion test serve to estimate the probability of explicit and implicit memory in our group of patients. Buchner *et al.*[15] describe the response behavior for targets and distractors in the inclusion and exclusion parts in terms of a series of successive steps. The parameters of the model indicate the corresponding probabilities. The first step for targets in both the inclusion and the exclusion parts depends on whether the patient has explicit memory (*i.e.*, parameters e and $1 - e$). The next step involves implicit memory. Implicit memory can be observed only if there is no explicit memory because the latter generally is assumed to overrule implicit memory effects. The parameter for this level is i. In the case of absence of both types of memory, the response in the stem-completion test is assumed to depend on guessing. The corresponding parameters are g and h for the inclusion and exclusion parts, respectively. The probabilities for explicit and implicit memory are iden-

Table 2. Hit Frequencies and Hit Rates for Targets and Distractors in the Inclusion and Exclusion Part of the Word-Stem Completion Test

	Inclusion Targets	Inclusion Distractors	Exclusion Targets	Exclusion Distractors
Hit frequency	7	59	44	53
Hit rate	0.370	0.307	0.229	0.276

Because 24 patients completed word stems in each of the four test conditions, n = 24× 8 = 192. Hit rates are derived by dividing the observed frequency by n.

tical in the inclusion and exclusion conditions. Because the test instructions are different, however, the expected responses are different: For inclusion target words, the branch with probability e leads to stem completion with target words (*i.e.*, hits), whereas, in the exclusion condition, this branch leads to completion with new words (*i.e.*, misses). In this way, the parameters e and i can be estimated. Data are expressed as the mean (± SD). $P < 0.05$ was considered to be statistically significant.

Results

Age of the patients was 24.3 ± 4.9 yr. The duration of surgery was 53 ± 12 min, and the interval between surgery and memory testing was 6.1 ± 2.4 h. The BIS during word presentation was 76.3 ± 3.0. All patients completed the structured interview concerning pre-, intra-, and postoperative recall. None of the patients claimed to have spontaneous recall of intraoperative events.

The hit frequencies and corresponding hit probabilities for targets and distractors in the inclusion and exclusion test are shown in table 2. The target hit rate in the inclusion part proved to be significantly larger than 0.3 (base-rate completion), whereas, in the exclusion part, the target hit rate was significantly lower than 0.3. However, the observed base rate in the inclusion part was somewhat higher (0.307) and in the exclusion part was lower (0.276; table 2 1) than 0.3. Although these differences were not significant, they might indicate a tendency of patients to use different strategies in the two parts of the test (*e.g.*, use unusual words in the exclusion part to decrease the possibility of using words presented during surgery). To reject the possibility of response bias, additional binomial tests were conducted, which showed that the target hit frequency in the inclusion test is statistically significantly higher than the base rate, even considering a higher base rate of 0.307. In the exclusion test, the difference between the target hit frequency and a base rate of 0.276 was not significant. This latter result might indicate that patients used unusual words in the exclusion part. *Post hoc* comparison of word frequency revealed, however, no significant differences between the inclusion and exclusion tests, which is indicative of no response bias.

Estimation of the Buchner *et al.*[15] model revealed a significant probability of explicit memory: The parameter for e equaled 0.112 (standard error = 0.064). The parameter for implicit memory in the absence of explicit memory was zero, indicating that the responses in the word-stem test resulted from either explicit memory or guessing. During testing, none of the patients was able to recall the words presented during surgery when presented with the word stem aurally and visually (*i.e.*, no cued recall).

Discussion

Memory during general anesthesia has been studied extensively.[16-21] Previous studies often have focused on investigating a single aspect of the relation between hypnotic depth and explicit and implicit memory; namely, studying implicit memory in a group of patients with a restricted range of hypnotic depth. Because of the restricted range, inferences in these studies are limited to whether implicit memory is evident in that particular group of patients. In addition, a common assumption in these studies is that so-called implicit memory tests are pure measures of implicit memory, *i.e.*, that they are not influenced by explicit memory. In our previous study of anesthetized patients undergoing trauma surgery, this assumption was avoided, and several aspects of the relation between memory function and hypnotic state were investigated simultaneously.[14] Explicit and implicit memory were separated using the PDP, and a model that relates both types of memory to depth of hypnotic state was shown to provide a satisfactory description of the data. Investigation of the dependence of memory on hypnotic state was possible because hypnotic state varies considerably in trauma patients. The probability of implicit memory was shown to decrease with increasing depth of hypnotic state. In that study, the mean BIS was 54, and no reliable evidence for explicit memory was found.

The current study complements the previous study[14] to the extent that we studied patients who, on average, had lighter levels of hypnotic state than patients in the trauma study. We used the same stimulus material and memory test. The main differences between the studies concern the anesthetic procedure and the finding that patients in the current study did not display large variations in hypnotic depth. Before integrating the results of both studies, we first discuss the results of the current study.

The current study shows that, after intraoperative word presentation at BIS values consistently greater than 70, patients had higher hit rates compared with base-rate performance in the inclusion part of the test. In the exclusion part, hit rates were lower. Hence, patients were able to make correct inclusion-exclusion decisions. None of the patients in the current study was able to consciously recall the words presented during surgery when seeing and hearing the first three letters of a word during testing. Apparently, patients made correct inclusion-exclusion decisions without being conscious of it. Nevertheless, making correct decisions resulted in a significant probability of explicit memory in the Buchner *et al.*[15] model. Explicit memory usually is thought to be a conscious form of memory (*e.g.*, persons know when and where they have learned the memorized information) and is opposed to implicit memory, which can occur in the absence of conscious recall.[22] However, our results show that explicit memory in the Buchner *et al.*[15] model is not synonymous with conscious recall; hence, the term "explicit" in the Buchner *et al.*[15] model is somewhat misleading. Surely, the PDP in combination with the Buchner *et al.*[15] model can measure conscious recall if present, but apparently this is not the only form of memory that affects the probability of explicit memory. Some unconscious form of memory that enables patients to make correct inclusion-exclusion decisions is part of the probability of explicit memory in the Buchner *et al.*[15] model as well. Because decision-making involves some control of memorized information, we suggest that this form of memory be called "unconscious-controlled memory." The Buchner *et al.*[15] model does not allow dissociation between conscious recall and unconscious-controlled memory; both forms of memory are measured by the parameter *e* for "explicit memory" in the Buchner *et al.*[15] model. We needed to ask patients to report each recalled word during testing to ensure absence of cued recall. The Buchner model, however, allows dissociation between unconscious-controlled memory and implicit memory. The latter can be conceptualized as being unconscious and uncontrolled. In the current study, we did not find evidence for conscious recall, but we found evidence for unconscious-controlled memory.

In the trauma study,[14] application of the Buchner *et al.*[15] model resulted in a nonsignificant probability of explicit memory; there was no convincing evidence for either conscious recall or unconscious-controlled memory. There was, however, evidence that implicit memory decreased with increasing depth of hypnotic state. Results from both studies are consistent with the hypothesis that all three forms of memory depend on depth of hypnotic state. The finding that trauma patients and those who underwent cesarean section had no conscious recall can be regarded as evidence that this form of memory is the first to be suppressed with increasing depth of hypnotic state. The finding that unconscious-controlled memory was preserved in patients who underwent cesarean section but not in trauma patients, in combination with the finding that BIS was, on average, greater during cesarean section might indicate that unconscious-controlled memory decreases before implicit memory. Note, however, that the anesthetic procedure differed in the two studies, which renders a direct comparison of the findings problematic. There is evidence that the relation between memory impairment and BIS varies slightly among different anesthetic drugs.[23] In addition to the difference in administered drugs, none of the BIS levels of the trauma patients stayed high throughout surgery. On the contrary, word presentation at high BIS values usually occurred at the beginning of an operation. All patients received adequate anesthesia after they were stabilized, which might have interfered with memory formation for the words presented earlier at a high BIS value. This might explain why trauma patients were not able to make correct inclusion-exclusion decisions, even for words presented at a high BIS value. Still, the fact remains that the results of both studies are consistent with the hypothesis that memory is dependent on the level of hypnosis during word presentation.

In summary, patients undergoing emergency cesarean section can correctly complete word stems with words presented during surgery (inclusion test) or avoid the presented words (exclusion test) if instructed to do so. Patients were not conscious that they made correct decisions in completing the word stems. Word presentation during surgery for these patients was consistently at BIS values greater than 70. Findings of our previous study[14] indicate that trauma patients, who had, on average, lower BIS values during word presentation, were not able to make correct inclusion-exclusion decisions. The results are consistent with the hypothesis that the sort of postoperative memory performance depends on the level of hypnotic state during word presentation. In neither of the studies were patients able to consciously recall words presented during surgery, even if the BIS was greater than 70. Considering the variation of memory test performance among patients, which was especially obvious in the trauma study, it would be interesting to focus future research on individual differences relevant in the context of memory for intraoperative events, such as speed of information processing, preoperative memory test performance, and drug tolerance.

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