An Investigation of Learning during Propofol Sedation and Anesthesia Using the Process Dissociation Procedure

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Background: **Many studies have shown that patients may remember words learned during apparently adequate anesthesia. Performance on memory tests may be influenced by explicit and implicit memory. We used the process dissociation procedure to estimate implicit and explicit memory for words presented during sedation or anesthesia.**

Methods: **We investigated intraoperative learning in 72 women undergoing pervaginal oocyte collection during propofol and alfentanil infusion. One word list was played once before infusion, another was played 10 times during surgery. Venous blood was taken for propofol assay at the end of the intraoperative list. Behavioral measures of anesthetic depth (eyelash reflex, hand squeeze response to command) were recorded and used to adjust the dose of anesthetic where clinically appropriate. On recovery, memory was assessed using an auditory word stem completion test with inclusion and exclusion instructions.**

Results: **The mean blood propofol concentration was 2.5 μg/ml (median, 2.3 μg/ml; range, 0.7–6.1 μg/ml). Mean alfentanil dose was 2.1 mg (median, 2.0 mg; range, 1.2–3.4 mg). Comparison of target and distractor hits in the inclusion condition showed memory for preoperative words only. However, the process dissociation procedure estimates showed explicit (mean, 0.18; $P < 0.001$) and implicit (mean, 0.05; $P < 0.05$) memory for the preoperative words, and a small amount of explicit memory for the intraoperative words (mean, 0.06; 95% confidence interval, 0.01–0.10). Memory performance did not differ between the 17 patients who consistently responded to command and eyelash reflex and the 32 patients who remained unresponsive. Blood propofol concentration and alfentanil dose did not correlate with memory for the intraoperative list.**

Conclusions: **There was no unprompted recall of surgery, but the process dissociation procedure showed memory for words presented during surgery. This memory was apparently explicit but did not correlate with the measures of depth of anesthesia used. (Key words: Awareness; memory; recall.)**

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MUCH human learning is explicit in that it is accompanied by awareness of the information being learned. However, learning without awareness, called implicit learning, may occur if information is presented too quickly for conscious perception[1] or if the learner is unconscious. Memory for learned information may also be explicit or implicit. Explicit memory is accompanied by awareness; in this situation, a conscious feeling of remembering such as one has when recollecting a holiday or recognizing a face. Implicit memory is a change in behavior or performance without conscious recollection or recognition of the event causing the change.[2] Implicit memory for a list of words may be assessed by a word stem completion task. Rather than being asked to recall words, the subject reads or listens to word stems, such as TRA-, and responds with the first word they think of that completes the stem (*e.g.,* TRACTOR). Implicit memory is inferred from the increased tendency to respond with words from the original list.

The relation between learning and memory is not simple. Explicit learning may result in explicit memory—for example, learning a volume of text and recalling it in an examination. However, sometimes explicit learning results only in implicit memory, especially if the subject was distracted during learning or if the test is carried out in a setting different from that in which the information was learned with few cues to aid explicit recollection.

Many investigators have demonstrated learning during apparently adequate anesthesia by playing word lists during anesthesia and asking patients to complete a test of implicit memory after recovery.[3–5] This learning has often been assumed to be implicit, but this is not a safe assumption for several reasons. First, it is difficult to ensure a constant level of anesthesia, particularly without depth-of-anesthesia monitoring; therefore, patients conceivably learned explicitly during undetected moments of consciousness. Second, explicit memory has often been ruled out because patients had no recollection of surgery, but free recall is an insensitive measure of explicit memory. Third, memory tests are not "process pure"; performance may be influenced by both explicit and implicit memory. Evidence for explicit memory would suggest that patients had been consciously aware of the intraoperative stimuli.

The process dissociation procedure is a method for determining the relative contribution of explicit and implicit memory to memory test scores.[6,7] It is widely used in psychological studies of implicit and explicit memory,[8–10] although it has been criticized for its assumption that implicit and explicit processes contribute independently to memory performance.[11] Rather than administering separate tests of implicit and explicit memory, the process dissociation procedure requires subjects to attempt a single test under two different conditions. In both conditions, subjects use the presented information (*e.g.,* word stems) to help them recall words they heard or saw earlier. In the inclusion condition, they use the recalled words to complete the test if possible; otherwise, they respond with the first word that comes to mind. In the exclusion condition, they are forbidden to use the recalled words and must instead respond with words that were not presented earlier. Thus, explicit recall aids performance in the inclusion condition but hinders it in the exclusion condition, whereas implicit memory always aids performance by increasing the likelihood of responding with a word learned earlier. The relative contribution of explicit and implicit memory to test performance is estimated by comparing the scores in the two conditions (see Appendix).

We used the process dissociation procedure to investigate the extent and type of intraoperative learning in lightly anesthetized and sedated patients undergoing minor surgery. Patients did not receive neuromuscular blockade; therefore, we assessed depth of anesthesia by recording hand-squeezing responses to command and eyelash reflexes before and after presentation of the stimulus words.

Materials and Methods

Approval for the study was granted from the Ethical Committee at Southmead Hospital, Bristol, United Kingdom. All women attending for pervaginal oocyte collection as part of *in vitro* fertilization treatment on the days when the principal investigator (Dr. Stapleton) was on duty were considered for the study. Exclusion criteria were perceptible hearing loss, language difficulties, neurologic dysfunction, and treatment with drugs affecting the central nervous system. We obtained informed consent from 78 women.

All patients received a mixture of propofol and alfentanil, but the infusion mixture and rates varied such that approximately one half of the patients were lightly anesthetized and one half were sedated (see Anesthetic Technique). The memory testing method was identical for all patients.

Anesthetic Technique

All patients were given 1 g paracetamol (acetaminophen) orally 30 min prior to surgery. In the operating room, intravenous access was established and monitoring of noninvasive blood pressure, pulse oximetry, and electrocardiography commenced.

All patients received an infusion mixture of propofol and alfentanil delivered from an Ohmeda 9000 infusion pump (Keighley, United Kingdom).

Forty-one patients received a mixture of 9 mg/ml propofol and 0.05 mg/ml alfentanil. Following an induction dose of 0.15 ml/kg body weight, a stepwise manual infusion scheme was used.[12,13] The infusion rate was $0.75\ \text{ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ for the first 10 min, $0.6\ \text{ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ for the second 10 min, and $0.45\ \text{ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ for the final stage. Increasing increments of 1 ml were given if patients moved during surgery.

Following a change in hospital policy unrelated to the present study, 37 patients received an infusion mixture of 8 mg/ml propofol and 0.1 mg/ml alfentanil. The induction dose was 0.1 ml/kg, and the infusion rates were 0.5, 0.4, and $0.3\ \text{ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ for the first 10 min, the second 10 min, and the final stage, respectively. Increments of 1 ml were given if needed to maintain a level of sedation and analgesia such that patients were comfortable but opened their eyes in response to command. Local anesthetic was not used.

Patients breathed spontaneously. Oxygen was delivered at 4 l/min *via* a face mask; an oral airway was used if necessary. After induction but before surgery, a 22-gauge intravenous cannula was placed in the antecubital fossa of the arm opposite to the infusion site to provide access for blood sampling. Surgery began 5 min after the induction dose was given.

Construction of the Memory Test

A list of 128 "parent" words, each having a different stem, was recorded by the second author onto a Macintosh computer (Apple Computer Inc., Cupertino, CA) using SoundEdit software (Macromedia Inc., San Francisco, CA). In a copy of this list, the tails of the words were removed to leave word stems of several phonemes. The word stems were tested by asking 12 undergraduate pilot subjects to listen to them played on an audio cassette player (Sanyo MCD-Z37L; Sanyo Electric Co., Osaka, Japan) and respond to each stem with "the first appropriate word that came to mind." We excluded all the stems to which nobody responded with the parent word, more than nine people responded with the parent word, or more than three people responded with a word that did not fit the stem.

The parent words belonging to the remaining 72 stems were assigned to three study lists so that the probability of those words being generated in response to their stems was equal in each list. The study lists were recorded on audio-tape with 1.5 s between words; the order of the words in each list was randomized. There were two versions of each study list. The preoperative version, which was presented once only, began with three practice words, separated from the main study list by a beep and ended with a beep. The practice words gave an opportunity for the patient to adjust the volume of the tape. The intraoperative list comprised only the study words, with no practice words and no beeps, allowing the list to be presented 10 times without interruption. The main investigator was blinded to the contents of the lists.

The stems of the words from each study list were assigned to two test lists such that the number of stems from each study list and the mean response probability were equal in each test list. The order of the 36 stems in each test list was randomized. The test lists were recorded on audio-tapes with 10-s intervals between stems to allow patients time to respond.

Stimulus Presentation and Intraoperative Data Collection

Each patient heard one of the study lists before surgery while fully conscious and another list during surgery while sedated or anesthetized. All lists were played from an audio cassette player through closed headphones (Sony MDR-V400; Sony, Tokyo, Japan). The preoperative list was played once, immediately before induction, and was preceded by a request to "Listen carefully to the list and try to remember these words."

The intraoperative list was played 10 times (taking 6 min), beginning immediately after the start of surgery. Before the start of the lists, the investigator reassured the patient by saying "Everything is going very well (patient's name). Listen carefully to the list and try to remember these words."

Response to the command "squeeze my fingers with your left hand," and eyelash reflex were recorded at the start and end of the intraoperative word list. Five milliliters of venous blood were collected at the end of the word list. The blood was stored at −4°C in oxalate. Blood propofol assay was performed using high-performance liquid chromatography with fluorescence detection.[14]

Each patient received two of the three study lists, one before anesthesia and one during surgery. The third list provided the distractor items for the memory test. The use of the lists as preoperative, intraoperative, or distractor lists was counterbalanced among patients.

Memory Testing

The postoperative memory test was performed on the ward when the patient had fully recovered from the anesthetic. The two test lists were presented using the same headphones and cassette player as before, and the subjects wrote their responses onto standard forms, in the presence of the investigator. One test list contained the stems of half the words from the distractor list and half the words from each of the two study lists; the other test list contained stems from the remaining study and distractor words. The patient's basic task was to complete the word stems. For example, they might complete the stem "TRA-" with the word "TRACTOR" or "TRANSPORT." However, in accordance with the process dissociation procedure, word stems from one list were completed under inclusion instructions, whereas word stems from the other list were completed under exclusion instructions. The inclusion instructions asked patients to use the word stem to help them recall a word they had heard earlier, and to write that word on the response sheet. If they could not remember hearing a word beginning with that stem, they should write the first word that came to mind which completed the stem. The exclusion instructions required them to use the word stem to help them recall a word they had heard earlier so they could avoid using words presented previously to complete the stems. Instead, they should complete the stem with the first nonrecalled word that came to mind. Each patient completed both test lists, one with inclusion and one with exclusion instructions. The order of the test lists and the order of the test conditions were counterbalanced among patients.

Statistical Methods

The memory test was scored in terms of "hits," that is, completions of stems with their parent words. Related-samples t tests were used to compare the proportion of hits from the presented lists with hits from the distractor list in the inclusion and exclusion conditions. Explicit and implicit memory were then estimated using the equations of Jacoby *et al.*[7] (see Appendix), and one-sample t tests were used to test whether the derived memory scores differed from zero. Independent-samples t tests were used to compare memory scores in patients who responded to command with those who did not. Multiple regression was used to test the relation between memory scores and anesthetic variables. Statistical significance was assessed with $\alpha = 0.05$. We applied the Bonferroni correction to keep family-wise α at 0.05 whenever the same statistical test was applied to both implicit and explicit memory for a particular word list. All analyses were performed using StatView 5.0 (SAS Institute Inc., Cary, NC).

The process dissociation procedure requires that participants respond consistently to nonremembered items. However, some people tend to be too cautious in the exclusion condition, excluding all familiar words rather than just the words they remembered hearing. Participants using this strategy can be detected by comparing performance on the distractor items. Those with baseline scores that differ widely in the two conditions are conventionally excluded from further data analysis.

Results

Data from four patients were excluded because their baseline performance differed by more than two standard deviations (five items) between the inclusion and exclusion conditions. Two other patients were excluded, one because she was too nauseous to complete the memory test and another because she responded

Table 1. Patient Characteristics, Duration of Surgery, and Time to Testing

	Mean	SD	Range
Age (yr)	34.1	5.1	24–45
Weight (kg)	65.0	11.3	47–106
Duration of surgery (min)	20	8	10–45
Time to testing (min)	119	45	40–260

with words that were not completions of the stems presented. This left 72 patients, 36 of whom had received the anesthetic infusion protocol and 36 of whom received the sedative protocol.

Table 1 shows patient characteristics, duration of surgery, and time to testing. The mean blood propofol concentration at the end of the list was 2.5 μg/ml (median, 2.3 μg/ml, range, 0.7–6.1 μg/ml). The mean total dose of alfentanil given was 2.1 mg (median, 2.0 mg; range, 1.2–3.4 mg). Depth of sedation–anesthesia varied among patients. Seventeen patients responded positively on both the eyelash reflex and hand squeezing tests at both the start and end of the intraoperative word list. Thirty-two patients gave no response at either time. The remaining patients responded to only one command or at only one of the times.

Memory Test Results

No patient had unprompted recall of events during surgery. Hit rates for the distractor list were comparable in the inclusion and exclusion conditions ($t < 1$), confirming that patients responded consistently on the two versions of the test. Memory for the preoperative and intraoperative word lists can be assessed in two ways: by comparing the proportions of hits for each list in the inclusion condition with those for the distractor list in the inclusion condition, and by using the proportions of hits in both conditions (inclusion and exclusion; table 2) to calculate explicit and implicit memory using the equations of Jacoby *et al.*[7] (see Appendix).

For the inclusion condition, patients scored significantly more hits for the preoperative word list than for the distractor list (related-samples t test, $P < 0.001$). Hits for the intraoperative list did not differ significantly from distractor hits, indicating that patients had no memory for the intraoperative word list. In the exclusion condition, hits for both presented lists were similar to those for the distractor list. Note that this result is ambiguous on its own; it may reflect lack of memory or it may reflect equal amounts of explicit and implicit memory because the two types of memory act in opposition in the exclusion condition, with implicit memory increasing hits and explicit memory decreasing hits. The main purpose of the exclusion scores is for calculating explicit and implicit memory.

For the preoperative word list, explicit and implicit memory estimates were statistically greater than zero even when the significance level was adjusted to 0.025 in accordance with the Bonferroni correction (one-sample, two-tailed t tests, $P < 0.001$ for explicit and $P = 0.013$ for implicit). For the intraoperative list, only the explicit memory estimate exceeded zero ($P = 0.012$).

We analyzed the effect of depth of anesthesia on memory for intraoperative stimuli in two ways. First, we compared explicit memory scores for the 17 patients who responded positively to both command and eyelash reflex at both the start and end of the intraoperative list with those for the 32 patients who never responded positively (implicit memory scores were not analyzed because they did not exceed zero). The difference between the means was not significant, and in fact, the nonresponders had a numerically higher mean (0.09) than the responders (0.02). Second, we entered blood propofol concentration and total dose of alfentanil into a multiple regression analysis, with explicit memory for the intraoperative list as the dependent variable. Propofol and alfentanil together did not contribute significantly to explaining the variance in memory for the intraoperative list ($R^2 = 0.02$), and neither correlated significantly with explicit memory for the intraoperative list (regression coefficients = 0.02 and −0.02, respectively).

The time between presentation of the intraoperative list and memory testing did not correlate with explicit memory for the intraoperative words (Pearson r = −0.08).

The preoperative word list mainly served as a check that the memory test was sensitive to memory and as a way of making the testing procedure meaningful to patients by ensuring they remembered some of the exper-

Table 2. Mean Probability of Hits in the Two Test Conditions and Mean Proportion of Explicit and Implicit Memory for Word Lists Played Preoperatively and Intraoperatively

	Mean Probability of Hit (± SD)		Mean Memory Estimate (± 95% CI)	
List	Inclusion Condition	Exclusion Condition	Explicit Memory	Implicit Memory
Preoperative	0.47 (0.20)	0.29 (0.14)	0.18 (0.13–0.24)	0.05 (0.01–0.08)
Intraoperative	0.33 (0.17)	0.27 (0.16)	0.06 (0.01–0.10)	−0.03 (−0.06–0.01)
Distractor	0.32 (0.16)	0.30 (0.13)		

CI = confidence interval.

imental stimuli. It also provides information about patients' ability to recall information presented to them immediately before their operation. We therefore repeated the above analyses on memory scores for the preoperative word list. Explicit memory for the preoperative words differed between the patients who consistently responded to command and those who did not respond ($P < 0.01$), with the nonresponders having the higher scores (0.23 compared with 0.04). Implicit memory scores did not differ between these two subgroups. Propofol and alfentanil doses did not explain a significant proportion of the variance in explicit memory ($R^2 = 0.03$) for the preoperative list. They did explain a significant proportion of the variance in implicit memory for the preoperative list ($R^2 = 0.13$; $P < 0.05$), with alfentanil making the greater contribution (regression coefficient for alfentanil = −0.11, $P < 0.05$; for propofol = 0.01). Time to test did not correlate significantly with explicit (r = −0.19) or implicit (r = 0.03) memory for the preoperative list.

Discussion

Patients received one list of words before sedation or light anesthesia with a propofol–alfentanil mixture and another list of words during surgery. On recovery, they completed a word stem completion test under the inclusion and exclusion instructions of the process dissociation procedure. Completion rates in the two conditions were used to calculate explicit and implicit memory. According to these calculations, patients had explicit and implicit memory for the preoperative words but only explicit memory for the intraoperative words. We expected patients to learn the preoperative word list because it was presented while they were fully conscious. The above-chance estimates of explicit and implicit memory for these words confirm that the word stem completion test picked up both types of memory. They demonstrate that patients can remember information presented immediately before induction of anesthesia. This is relevant because patients sometimes ask further questions about their surgery or anesthetic at this time. Patients who were more deeply anesthetized after hearing the preoperative list were more likely to have explicit memory for the list on recovery.

The process dissociation procedure measures explicit memory as the difference in hit rates between the inclusion and exclusion conditions. This difference was statistically significant for the intraoperative word list, indicating explicit memory for the words presented during surgery. This explicit memory enabled patients to use the previously presented words to complete the word stems in the inclusion condition and to avoid using them to complete stems in the exclusion condition. However, there was insufficient explicit memory to raise the completion rate for intraoperative words above that for the distractor words in the inclusion condition. Therefore it appears that patients had only a small amount of explicit memory for words played during surgery.

The finding that memory was explicit contrasts with many previous studies that claimed to show implicit memory for intraoperative stimuli in the absence of explicit memory. Often, these studies assessed explicit memory by asking patients if they could remember anything that happened during anesthesia. We used a stem completion task that is more sensitive because it provides some cues (*i.e.,* word stems) to help patients retrieve explicit memories. Thus, we may have demonstrated explicit memory when others failed to do so because we used an easier memory test. Additionally, a possible reason for patients failing to recollect intraoperative stimuli is that they believe they will remember nothing about surgery, and therefore have little incentive to try and recall the word list. An important feature of our study is the inclusion of a preoperative word list. Because patients remembered some words from this list, the whole memory testing procedure should have seemed more meaningful to them.

Therefore, we may have observed explicit memory for intraoperative words because we used a memory test that is more sensitive than the frequently used task of asking patients to recall surgery. However, the finding that memory for the intraoperative words was explicit rather than implicit sits awkwardly with the finding that it was not sensitive to depth of anesthesia. Explicit memory is typically very sensitive to manipulations of consciousness,[15] yet we observed as much explicit memory in patients who were unresponsive to commands during list presentation as we did in patients who remained responsive. Likewise, memory performance did not correlate with dose of propofol and alfentanil.

Lubke *et al.*[16] studied learning during emergency cesarean section under general anesthesia with nitrous oxide, isoflurane, and morphine. Like us, they reported explicit memory for intraoperative stimuli but no implicit memory. They too used the process dissociation procedure with auditory word stem completion, although they used a multinomial processing model[17] to estimate implicit and explicit memory rather than the more conventional analysis used in our study. They also asked patients to report any words they consciously recalled when the word stems were presented. No patient recalled any of the words, despite having some memory which enabled them to include or exclude those words appropriately during the word stem completion task. Lubke *et al.*[16] argued that patients could include and exclude the words, despite absence of explicit recall, because they had "unconscious–controlled" memory but not the "unconscious–uncontrolled" memory that is the usual conception of implicit memory. In other words, they were able to use their implicit memory deliberately during the memory test, even though they were unaware of that memory. Although this is an interesting explanation of their finding, and possibly of ours as well, it does not fit easily with current theories of memory.

In the exclusion condition, patients should have used the word stems to recall previously presented words and avoided using recalled words as responses. Use of an alternative strategy may have led us, and Lubke *et al.*,[16] to overestimate explicit memory at the expense of implicit memory. This alternative strategy is to generate words that fit the stems, then exclude any words that are recognized from earlier in the study. This generate–recognize strategy produces unreliable estimates of implicit and explicit memory because: (1) applying the equations of Jacoby *et al.*[7] is inappropriate because patients are using explicit and implicit memory in conjunction rather than independently;[18] and (2) recognition may be influenced by both explicit and implicit memory (the latter contributing a feeling of familiarity), yet successful exclusion of targets only increases the estimate of explicit memory. We tried to minimize the danger of patients using a generate–recognize strategy by emphasizing the importance of recalling previously presented words before deciding to include or exclude, and by using a preoperative list to ensure that patients had clear explicit memory for some words.

Nonetheless, the conclusion that the patients in our study had explicit memory for intraoperative words must be treated with caution. If the finding is taken at face value, then because explicit memory results only from explicit learning, it suggests that patients only learned words during surgery when they were conscious of them. This finding supports the hypothesis that learning occurs only when anesthesia is light enough to permit moments of awareness. Previous studies have found memory for intraoperative stimuli without explicit recall of surgery, but few attempted to define consciousness by using depth-of-anesthesia monitoring, and few used sensitive tests of explicit memory. The apparent persistence of implicit memory formation in those studies may in fact reflect explicit learning of stimuli presented during moments of consciousness. Two studies tentatively support this conclusion. Schwender *et al.*[19] examined mid-latency auditory evoked potentials and learning in patients undergoing cardiac surgery. The waveform of the mid-latency auditory evoked potentials in the patients who learned was very similar to the awake waveform. Russell and Wang[20] used the isolated forearm technique with explicit and implicit memory testing in patients who were anesthetized and paralyzed for gynecological surgery. No patient responded to command or had any demonstrable memory for words presented during surgery.

The small amount of learning during propofol anesthesia in the current study is consistent with the demonstration by Cork *et al.*[21] of learning during surgery with conscious propofol sedation. In contrast, a volunteer study[22] found no learning during propofol sedation that was light enough to preserve short-term memory function and response to command. A subsequent patient study failed to find learning during propofol sedation or light anesthesia immediately before surgery.[23] Polster *et al.*[24] did demonstrate learning during propofol sedation in volunteers, but sedation in their study was so light that subjects were able to sit up and complete a computerized test. Each of these studies used a different memory test, so they are not directly comparable. However, we offer a speculative explanation of the overall pattern of data, namely that the probability of learning varies with the presence or absence of surgery as well as with depth of sedation or anesthesia. Surgery may facilitate learning by increasing levels of circulating catecholamines, which are known to modulate learning.[25–27] There is some evidence from animal studies that epinephrine enables learning during anesthesia,[28–30] although El-Zahaby *et al.*[31] failed to replicate this finding.

Lubke *et al.*[32] recently studied learning during isoflurane anesthesia in trauma patients. There are interesting similarities and differences between their study and ours. They used essentially the same memory testing procedure and, despite testing several days rather than hours after surgery, they found similar levels of explicit memory for intraoperative words. Using the model of Buchner *et al.*,[17] they estimated the probability explicit memory as 0.06, which, although of similar magnitude to our estimate, was not statistically significant. Applying the equations of Jacoby *et al.*[7] to their mean hit rates gives a rough estimate of 0.05, which is slightly lower than our estimate. Lubke *et al.*[32] also found implicit memory for intraoperative stimuli (0.10, from the model of Buchner *et al.*[17]). Bispectral index values during word presentation correlated significantly with subsequent word memory ($R^2 = 0.12$), confirming that the probability of learning increases as depth of anesthesia decreases. A possible explanation of the different outcomes in the study of Lubke *et al.*[32] and our study is that propofol impairs learning more effectively than isoflurane, but evidence is mixed in this regard. Learning has been demonstrated during anesthesia with propofol[33] and with isoflurane,[34,35] but other authors have found that no learning occurs with these drugs.[19,36] Our speculative hypothesis that surgery contributes to learning by raising catecholamine levels offers another potential explanation. Catecholamine levels were possibly high, and variable, in the trauma patients of Lubke *et al.*,[32] and this variation in catecholamine levels may explain additional variance in memory performance. Although bispectral index predicted memory performance, it did so weakly, leaving 88% of the variance in memory unexplained. We hope that, by testing this hypothesis, future research regarding learning during anesthesia will move away from simply trying to demonstrate learning and toward an analysis of the anesthetic and physiologic conditions under which learning does and does not occur.

We found weak evidence for learning during surgery with light anesthesia or sedation. Our memory test results indicated that learning was conscious, but the lack of sensitivity of learning to depth of anesthesia suggests that learning was unconscious. We speculate that the relation between consciousness and learning appears complex because surgical stimulation influences the probability of learning by increasing catecholamine release as well as by decreasing depth of anesthesia.

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Appendix: Derivation of the Equations to Estimate the Contributions of Implicit and Explicit Memory to Performance on the Word Stem Completion Task[7]

$$\text{Explicit memory} = \text{inclusion test score} - \text{exclusion test score} \quad (1)$$

$$\text{Implicit memory} = \text{exclusion test score}/(1 - \text{explicit memory}) - \text{baseline response rate} \quad (2)$$

The probability of responding with a target word in the inclusion condition is the sum of the probability of explicit recollecting the word (R) and the probability of the word coming to mind automatically without recollection (A).

$$\text{Inclusion} = R + A(1 - R) \quad (3)$$

In the exclusion condition, responding with a target word occurs only when there is a failure to recollect the word explicitly but the word comes to mind automatically. Hence:

$$\text{Exclusion} = A(1 - R) \quad (4)$$

These two equations enable estimation of the probability of explicit recollection:

$$R = \text{inclusion} - \text{exclusion} \quad (5)$$

and of automatically responding with a word without explicitly recollecting it:

$$A = \text{exclusion}/(1 - R) \quad (6)$$

The probability of a target word automatically coming to mind is determined by implicit memory for the word and one's tendency to produce that word in response to its stem even in the absence of memory. Therefore:

$$\text{Implicit memory} = A - \text{baseline response rate} \quad (7)$$

Thus, combining the two equations:

$$\text{Implicit memory} = \text{exclusion}/(1 - R) - \text{baseline response rate} \quad (8)$$

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