Anesthesia: Biologic Foundations, edited by
Tony L. Yaksh et al. Lippincott–Raven Publishers,
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CHAPTER 28

MEMORY AND RECALL

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Among the most important clinical indices of general anesthesia is the patient's inability to remember, postoperatively, the events that transpired during his or her surgery. Patients who cannot remember such events, including sensations of pain and other experiences of distress, are held to have been adequately anesthetized. The central role played by memory in assessments of the adequacy of anesthesia lends great importance to understanding the nature of this mental faculty. This is especially the case, in view of emerging evidence that conscious recollection is not all there is to memory. The possibility that surgical events may be encoded in memory and expressed in postsurgical experience, thought and action, albeit outside of phenomenal awareness, poses both a special challenge and a special opportunity for anesthesiology. (For additional coverage of the literature on anesthesia and memory, see refs. 3,8,9,44,88,89,91,120,125,126,143,160. A great deal of related literature on awareness and depth of anesthesia is collected in refs. 101,116,169. Of special interest are the proceedings of the first and second international symposia on Memory and Awareness in Anesthesia, refs. 31,181. The third such symposium was held in Amsterdam in 1995.)

PSYCHOLOGY OF MEMORY

Memory refers to a mental faculty by which organisms form, retain, and use mental representations of the past. (For thorough treatments of the psychology of memory, see refs. 11,64,76,96,180,188; also see the periodic reviews appearing in the *Annual Review of Psychology*. For comprehensive treatments of cognitive psychology, see refs. 6,13,141. For a discussion of memory in a neuroscientific context, see refs. 87,175.) Put another way, memory refers to the means by which organisms encode, store, and retrieve knowledge acquired through experience. There is an intimate relationship between memory, perception, learning, and thought. Perception forms mental representations of current events; memory stores knowledge gleaned from the present for use in the future, when stored knowledge is retrieved and mental representations of past events are reconstructed. It is by means of learning that organisms acquire new knowledge and store it in memory. In the course of thinking, organisms use stored knowledge, retrieved from memory, in the service of judgment, reasoning, inference, and problem-solving.

Classification of the Contents of Memory

Not all stored knowledge is of the same type. Intuitively, there are qualitative differences among one's knowledge of English grammar or of the way to tie a Windsor knot, the meaning of words like hegemony or leitmotif, that Columbus landed in America in 1492 and that ether was introduced by Morton in 1846, one's first kiss and what one ate for dinner last Tuesday. In accordance with these intuitions, as well as a great deal of experimental evidence, psychologists often classify the knowledge stored in memory in terms of the hierarchy displayed in Fig. 1.

At the highest level of the hierarchy is the distinction between procedural and declarative knowledge (5,218). Declarative knowledge consists of facts or beliefs about the nature of the world: it can be represented in propositions, sentence-like statements consisting of two nouns (or noun phrases) and a verb (or verb phrase) expressing some relation between the noun phrases—for example, "The surgeon grasped the scalpel." Procedural knowledge, by contrast, consists of the skills, rules, and strategies by which we manipulate and transform declarative knowledge: it can be represented in productions, "if-then" statements consisting of a goal, a condition, and an action by which that goal can be achieved under that condition—for example, "If you want to tie a Windsor knot, then begin by bringing the long end of the tie in front of the short end; then bring the long end up through the loop."

The difference between declarative and procedural knowledge is the difference between knowing that and knowing how (170). Procedural knowledge can be further classified into cognitive skills (such as performing long division or taking square roots) and motor skills (such as playing piano or tennis). Some procedural knowledge is innate, but much of it is acquired through repeated practice. Once acquired, however, productions are executed automatically when their constituent goals and conditions are instantiated, without any conscious intent on the part of the person, and without consuming any attentional capacity. Once engaged, productions cannot be controlled until they have been discharged, and further, the person may be entirely unaware of their execution.

Declarative knowledge can be further classified into episodic and semantic forms (203). Episodic memory consists of autobiographical information: the individual's knowledge of specific events that have transpired in his or her lifetime. Semantic knowledge is the individual's mental dictionary (and encyclopedia) of abstract and categorical information about the world. Both episodic and semantic knowledge can be represented in propositions. But in the case of episodic knowledge, the proposition contains more or less concrete reference to the specific time and place at which an event occurred, as well as reference to the rememberer as the agent or experiencer of that event. Thus, our knowledge that Columbus landed in America in 1492 is a fragment of semantic memory; by contrast, our knowledge of the circumstances under which we acquired that bit of knowledge is a piece of episodic memory. Most, if not all, of our declarative knowledge is acquired through experience; but as the circumstances under which that knowledge is acquired

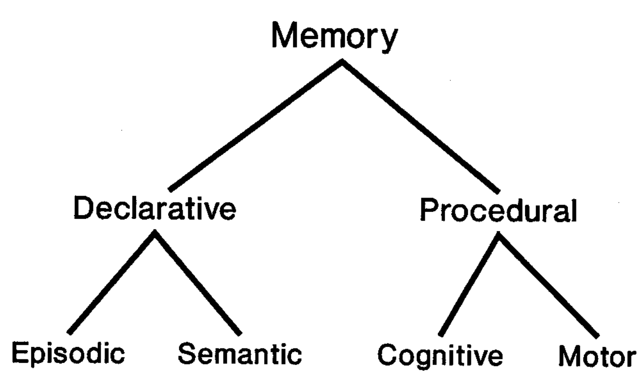

Figure 1. Hierarchical classification of knowledge stored in memory.

begin to blur and fade, episodic memories are transformed into semantic ones.

Consider the following report from the annals of neurology. While greeting a patient suffering amnesia from alcoholic Korsakoff's syndrome, Claparede (53; and for a discussion, see ref. 122) pricked her palm with a pin hidden in his hand. Claparede left the ward while the patient was placated, after which he returned and greeted her again. The patient had no memory for having met Claparede before, but declined to shake his proffered hand. When asked to justify her refusal, she replied only that people sometimes hide pins in their hands. Knowledge that people sometimes hide pins in their hands is a piece of semantic information, presumably acquired through direct or vicarious experience; knowledge of the occasion on which the patient was herself pricked is a piece of episodic information, representing the experience itself.

Processing of Memory

The distinctions between declarative and procedural knowledge, and between episodic and semantic knowledge, are highly relevant to the question of postoperative memory. When we ask whether a patient was adequately anesthetized, we ask whether he or she has any recollection of events (e.g., conversations among members of the surgical team) and experiences (e.g., feelings of pain) that transpired while he or she was in surgery. That is to say, we ask questions about the person's episodic memory. Understanding why certain events are remembered, and why others have been forgotten, has been a central task of cognitive psychology since the scientific psychology of memory began with the work of Ebbinghaus (70). This literature can be summarized as a series of nine principles governing remembering and forgetting (for more extended treatment of these principles, see ref. 123).

The analysis of memory is governed by an overarching framework known as the stage principle (64).

1. The stage principle. Any instance of forgetting can be attributed to a failure of encoding, storage, or retrieval, either alone or in combination.

Encoding is the process by which a trace of current experience is laid down in memory; storage, that by which an encoded memory trace remains available over time; and retrieval, the process of recovering information from storage for use in ongoing cognitive activity. In strictly logical terms, a memory cannot be retrieved from storage unless it was encoded in the first place, or if it was lost from storage after being encoded.

The encoding process itself is governed by two principles, elaboration (7,60,61) and organization (36,138).

2. The elaboration principle. The memorability of an event increases when that event is related to preexisting knowledge available at the time of encoding.

3. The organization principle. The memorability of an event increases when that event is related to other events occurring at the time of encoding.

Events are remembered to the extent that they were encoded at the time they occurred. Proper encoding does not occur automatically, but rather requires active, cognitive effort. This effort takes two forms (103): relating individual items to the base of preexisting knowledge already stored in memory (elaboration, or item-specific processing), and relating individual items to each other (organization, or relational processing).

Once a memory has been encoded, it is, at least in principle, available for subsequent retrieval and use. However, in practice memories seem to fade over time, an observation that has been enshrined in another principle (70):

4. The time-dependency principle. The memorability of an event declines as the length of the storage interval (i.e., the time between encoding and retrieval) increases.

Of course, there are instances in which knowledge appears to be preserved in rich detail over long periods of time, as in so-called "flashbulb" memories for emotionally arousing events (216), and the "permastore" of factual knowledge (12). But these are the exceptions that test the rule, and in any event careful studies have shown that many flashbulb memories are highly inaccurate, and the notion of a permastore generally refers to semantic rather than episodic memory.

The experimental literature does contain a number of studies of so-called hypermnesia, in which memory appears to grow rather than fade with time (77,123,156). This phenomenon appears to contradict the time-dependency principle, but in fact it is consistent with the elaboration, organization, and time-dependency principles. Hypermnesia occurs when items were subject to elaborative and organizational activity at the time of encoding, and most hypermnesia is accomplished on the first few attempts at retrieval, relatively soon after encoding has taken place.

The retrieval process itself is governed by a large set of principles, all of which follow from the general distinction between the availability and accessibility of items in memory storage (204):

5. The accessibility principle. An item that is available in memory storage is not necessarily accessible on every retrieval attempt.

For example, accessibility varies with the means by which retrieval is attempted. By and large, recognition tests produce more memory than recall tests, and cued recall produces more memory than free recall. This leads to another principle, directly governing the accessibility of items available in memory storage (202):

6. The cue-dependency principle. The memorability of an event increases with the amount of information supplied by the retrieval cue.

Remembering usually begins with some kind of cue that provides some information about the event which is to be remembered. Cues that are highly informative are more likely to contact available memory traces than those that are not. In some respects, encoding and retrieval are in a complementary relationship: access to well-encoded memories generally requires fewer retrieval cues, and a rich retrieval environment can promote access even to very poorly encoded memories.

Cues are important, but they must also supply the right kind of information, not just the right amount (206):

7. The encoding specificity principle. The memorability of an event increases when the information processed at the time of retrieval was also processed at the time of encoding.

The manner in which an event is encoded—the meaning of the event, how it is perceived, interpreted, and categorized—determines which retrieval cues will be successful in gaining access to that event. Encoding specificity appears to underlie the phenomenon of state-dependent memory—whether "state" is defined in physiological, emotional, or environmental terms.

Memory is also determined by the degree to which an event conforms to our expectations and beliefs (100):

8. The schematic processing principle. The memorability of an event increases when that event is relevant to expectations and beliefs about that event.

The general principle is straightforward enough, but the details may be a little surprising. If memory is plotted as a function of the degree to which the target events can be predicted on the basis of preexisting knowledge (represented in the form of organized knowledge structures known as schemata), it turns out that events that are highly congruent with expectations are also highly memorable; but events that are highly incongruent with active schemata are even more memorable. Events which are irrelevant to our expectations are generally unmemorable. The U-shaped function apparently reflects the operation of two different principles: events that are inconsistent with preexisting schemata are surprising and draw more attention, and thus receive more elaborative and organizational activity at the time of encoding; and at the time of retrieval, the relevant schema provides additional cue information that can facilitate access to relevant memories. Events that are irrelevant to the schema get neither advantage, and so are poorly remembered.

The role of cognitive schemata is also underscored by another principle (14):

9. The reconstruction principle. The memory of an event reflects a blend of information retrieved from specific traces encoded at the time of that event, with knowledge, expectations, and beliefs derived from other sources.

In describing how memory works, we often resort to the metaphor of a library: memory traces are books that must be purchased and catalogued; the prospective user must look up the book in the catalog in order to know where to find it; and in order for the search to succeed, the book must not have been eaten by worms, or displaced by a careless user. The library metaphor will take us a long way, but the notion of memory retrieval obscures the fact that memories can be distorted, biased, and otherwise altered by changes in perspective and other events that occur after the time of encoding. In the final analysis, memory is not so much like reading a book as it is like writing one from fragmentary notes. The reconstruction principle is of utmost importance in the present context, because it means that any particular memory is only partly derived from trace information encoded at the time of the event: in the process of remembering, trace information combines with knowledge, beliefs, and inferences derived from other sources.

Several of these principles of remembering and forgetting are directly relevant to the question of postanesthetic memory. For example, the accessibility and cue-dependency principles lead us to worry about the degree to which the usual tests of memory employed by anesthesiologists adequately assess any information patients have acquired during their surgical experience. To what extent is patients' performance on memory tests administered immediately after surgery affected by their incomplete recovery from general anesthesia, or the clouding of consciousness produced by postsurgical administration of analgesics such as morphine? Would the same test, administered after a delay, produce different results? In adequately anesthetized patients, tests of free recall generally yield nothing; but what might be revealed by other tests, such as cued recall and recognition? But if patients seem to remember more under conditions of cued recall and recognition than free recall, we have to worry about the reconstruction principle: to what extent do the patients' reports reflect the actual retrieval of memories, compared to plausible reconstructions based on information supplied in the investigator's queries?

The encoding specificity principle, which states that encoding conditions constrain the effectiveness of retrieval cues, has a number of implications for postsurgical memory. Consider first the principles governing memory encoding. The formation of a well-encoded (and thus long-lasting and easily retrievable) memory trace depends on elaboration and organization. These processes require the active deployment of attention—a degree of cognitive activity that is likely to be precluded by adequate general anesthesia. At the same time, however, the schematic processing principle holds that encoding is likely to be enhanced for events that are unexpected, personally relevant, and highly salient—which, in the surgical context, would seem most likely to include mishaps, accidents, and remarks about the patient. Accordingly, any memories retained from surgery are probably more likely to be negative (and litigable) than positive in character.

The encoding specificity principle raises the further, and somewhat disconcerting, question of whether memory for intraoperative events might not be state-dependent—that is, whether memories encoded during general anesthesia might be inaccessible in the normal waking state, but fully accessible if the patient is subsequently anesthetized. Beginning with the classic studies of Overton (154), a large empirical literature has documented state-dependent learning and memory (SDM) effects associated with a wide variety of psychoactive drugs including alcohol, barbiturates, caffeine, and marijuana (for reviews, see refs. 72,75,211). That is, if encoding takes place under the influence of a particular pharmacological substance, retrieval is more effective when the subject is under the influence of that same drug (or one with highly similar pharmacological properties). Could such a thing happen under anesthesia as well? This theoretical possibility would seem impossible to test, given the inability of adequately anesthetized patients to communicate with others (and thus complete memory tests) during surgery. Moreover, it should be remembered that most drugs which produce SDM also impair encoding and retrieval processes. Thus, even when both encoding and retrieval occur in the drugged state, memory is not as good as it would be in the absence of drugs. Thus, the practical consequences of state-dependent memory in general anesthesia would seem to be minimal. However, the possibility of state-dependency should not be discounted in cases where patients undergo surgery under lighter planes of anesthesia.

Explicit and Implicit Expressions of Episodic Memory

When we ask questions about postoperative memory, we usually ask about the patient's conscious ability to recollect intraoperative events. However, as Claparede's (53) case of Korsakoff's syndrome shows, it is possible for information relating to an episode to be retained in memory, and influence subsequent behavior, even though the episode itself is not remembered.

The influence of past experience on present behavior, in the absence of conscious recollection of that experience, is manifested on more formal tests performed on amnesic patients. For example, the patient H.M., who underwent surgical excision of the medial portion of his temporal lobes as a desperate treatment for intractable epilepsy, remembers nothing that has occurred since the date of his operation (57,146,179). Yet, he retains a number of perceptual-motor skills, including mirror drawing and pursuit-rotor learning, which were taught to him after his operation. Studies of other amnesic patients show similar selective effects on memory: in each case, procedural knowledge is acquired and retained, although declarative-episodic memory for the learning experience is lost. However, the fact that the skill has been retained means that some trace of the learning episode has been preserved as well.

The selective effects of amnesia can be demonstrated within the declarative domain itself. In a typical experiment, amnesic patients are asked to study a list of familiar words, such as motel or assassin. After a short period of distraction, they are unable to remember any of the words that appeared on the list. At this point, they are presented with stems (e.g., mot—) or fragments (e.g., a—a—in) and asked to complete them with the first word that comes to mind. In the case of word stems, which have many possible completions, amnesic patients are more likely to fill in the blanks with study items than are control subjects, who never encountered the list; in the case of word fragments, which have only a single possible solution, amnesic subjects are more likely to produce the target than controls. These outcomes (for example, see refs. 95,210) are generically known as priming effects. In fact, amnesics generally show the same degree of priming as normal subjects who remember the study list perfectly well.

Priming is most frequently observed on semantic memory tasks: subjects are asked to retrieve items from their mental lexicons rather to remember items that they have studied. However, not all priming is mediated by semantic knowledge. In repetition priming, presentation of an item at study facilitates the processing of that same item at test; in semantic priming, presentation of an item at study facilitates the processing of a semantically related item at test (there are also other forms of priming). Regardless of the nature of the priming, however, the effect is clearly attributable to the prior presentation of list items: thus, when priming occurs, it is because something of the episode has been preserved in memory.

The ability of amnesic patients to capitalize on prior episodes of study or learning, in the absence of any recollection of the episodes themselves, motivates a distinction between two expressions of memory: explicit and implicit (171–173). Explicit memory refers to conscious recollection, as indicated by the ability to recall or recognize an event from the past; in fact, explicit memory tasks require just such conscious recollection. Implicit memory, on the other hand, refers to any change in experience, thought, or action, such as priming effects, that is attributable to past events; in formal terms, implicit memory tasks do not require conscious recollection of the past. In fact, a large amount of evidence has accumulated that explicit and implicit memory can be dissociated in both amnesic patients and normals. That is, implicit memory can be spared even though explicit memory is grossly impaired.

Current theoretical accounts of implicit memory come in three basic forms, each with a number of variants (for fuller discussion, see refs. 94,114,134,164–167,171–173). According to the activation view, perceptual processing of an event activates preexisting internal representations of knowledge corresponding to the features of that event. This activation persists for some time after the event has passed, forming the basis for priming effects. According to the multiple systems view, explicit and implicit expressions of memory are supported by different physical systems in the brain. For example, explicit but not implicit memory may require involvement of the hippocampus. According to the processing view, explicit and implicit memory result from different kinds of operations performed on perceptual inputs. For example, explicit memory may require that the meaning of an event be processed, while implicit memory may require analysis only in terms of its physical properties.

Each of these views makes its own particular assumptions about how memory is structured. For example, the activation and processing views tend to assume that memory is a unitary storehouse of knowledge, whereas the multiple systems view assumes that there are many different kinds of memory. In addition, the activation view assumes that new events are encoded by recombining preexisting knowledge, while the multiple systems and processing views allow for the encoding of entirely new representations in memory. In principle, these sorts of differences create the possibility that experimental tests could indicate which view is correct, but in practice this sort of evidence has been difficult to produce. Moreover, some versions of each view include elements of one or more other views, making decisive tests difficult to conduct. For present purposes, it is the explicit-implicit distinction itself that is more important, because it raises the possibility that memories of surgical events may be encoded, retained, and expressed outside of awareness. The specific characteristics of implicit memory are important in interpreting the literature on implicit memory in surgical anesthesia, however, so we will return to this issue at the end of the chapter.

From Implicit Memory to Implicit Perception

In the usual case, implicit memory occurs for events that were consciously perceived at the time they originally occurred. Amnesic patients, for example, are aware of the target items at the time they study them, even if they forget them quite quickly thereafter. However, it is also possible to observe priming effects when the events were never perceived in the first place. In such cases, implicit memory provides evidence for implicit perception: a change in experience, thought, or action that is attributable to an event in the current environment, independent of conscious perception of that event (124). A great deal of evidence, involving both brain-damaged patients and intact subjects, shows that explicit and implicit perception can be dissociated in much the same way as explicit and implicit memory.

For example, patients suffering damage to the striate cortex report an inability to see objects presented in their scotoma; yet, in at least some cases, they are able to make "guesses" about the visual properties of stimuli that are more accurate than would be expected by chance—a phenomenon dubbed "blindsight" (212). Similarly, patients with lesions in the temporoparietal region of the right hemisphere fail to attend to objects in their left visual field; yet, again at least in some cases, their choice behavior is guided by information available in the neglected area. Among intact subjects, interest in so-called subliminal perception has been revived by compelling demonstrations of priming effects attributable to stimuli that are presented at intensities that are too low, or durations too short, to be consciously perceived (35,49,97,142,152).

One piece of evidence supporting the concept of implicit perception is a form of the mere exposure effect (222). In the typical mere exposure experiment, subjects receive repeated presentations of a list of unfamiliar items (e.g., pseudowords, nonsense drawings, or foreign words). They are then presented with list items, paired with previously unpresented control items, and asked to indicate which they prefer. On average, subjects prefer those items to which they had been previously exposed. The mere exposure effect is an expression of implicit memory, because the previous exposures have changed the person's response to the list items. Interestingly, the mere exposure effect occurs even if the initial presentation of the items was subliminal (129; for a review, see ref. 34). Because memory for an event requires that the event be perceived in the first place, in this case implicit memory simultaneously provides evidence for implicit perception: the subject's experience, thought, and action is influenced by visual events in the absence of conscious perception of those events.

The implication of the literature on implicit memory is that assessments of memory should go beyond what the person can consciously recall or recognize, to examine the possibility of remembering without awareness (71,107). In the same manner, the implication of the literature on implicit perception is that unperceived events can also leave traces in memory that affect subsequent behavior. Therefore, the possibility remains that, even though adequately anesthetized patients do not explicitly perceive surgical events (at least by the most generally accepted accounts of anesthesia) and, in any event, lack explicit memory for such events, careful testing might show that implicit memories of surgical events have been preserved.

This possibility is strengthened by the fact that at least some forms of implicit memory are not affected by the same sorts of factors (e.g., elaboration and organization) that govern the encoding of consciously accessible memories (171–173,205). Thus, implicit memory may occur even when a patient is unable to perform the kinds of cognitive operations usually considered necessary for the formation of an explicit memory. In the remainder of this chapter, we survey a rapidly developing literature which assumes that explicit memory is impaired by adequate anesthesia (as indeed it must be, by definition), and proceeds to inquire into the fate of implicit memory.

Notes on the Neuroscience of Memory

From a psychological point of view, an episodic memory may be described as a bundle of features, or a set of propositions, that describe some event or experience. A basic question for neuroscience concerns how such knowledge is encoded in the nervous system (for comprehensive reviews, see refs. 186,187,189). This question has been approached at a number of different levels. For example, studies of conditioning and learning in the marine mollusk aplysia have shed a great deal of light on the molecular basis of memory (117). Despite their very simple nervous systems, aplysia are capable of both nonassociative (habituation, sensitization) and associative (classical conditioning, and instrumental conditioning) forms of learning (for example, see ref. 43). The fact that aplysia neurons are both relatively few in number and relatively large in size permits detailed analysis of synaptic changes (known as short-term and long-term potentiation) occurring as a result of learning. Similar analyses have been carried out in a wide variety of species, suggesting that some physiological mechanisms of learning and memory are common to vertebrates and invertebrates.

Of course, studies of nonhuman animals cannot inform us of the biological substrates of conscious recollection, because we have no way of knowing whether, or to what degree, such animals are aware of what they have learned. However, such evidence is now available from two sources: neuropsychological studies of brain-damaged patients who display a dense anterograde amnesia known as the amnesic syndrome (182); and behavioral studies of monkeys and other primates in whom experimentally induced lesions seem to produce deficits in learning and memory analogous to those observed in the amnesic syndrome (147). The organic amnesic syndrome comes in two general forms: patients displaying Korsakoff's syndrome, such as the woman described by Claparede (53), have suffered damage to the midline portion of the diencephalon, including the dorsomedial thalamic nuclei and the mammillary bodies; in other cases, such as the patient H.M. (57,146,179), the damage is to the medial area of the temporal lobe, including the hippocampus, amygdala, and other adjacent areas. Diencephalic patients usually show damage to the frontal lobes and diffuse cortical atrophy as well, giving their amnesia special properties, such as anosognosia, confabulation, and metamemory deficits (149,183).

Once the memory deficit in question has been thoroughly described, anatomical and brain-imaging studies can be performed to determine which brain areas are involved. Recently, for example, Squire and Zola-Morgan (191; see also ref. 189) have offered evidence for a memory system located in the medial portions of the temporal lobe, which is important for the encoding and storage of declarative knowledge, both semantic and episodic. The system consists of the hippocampus, entorhinal cortex, perirhinal cortex, and the parahippocampal cortex. When these structures are damaged, perception and short-term memory are unaffected, but long-term memory is grossly impaired. Moreover, the long-term impairment affects explicit memory, but not implicit memory. The medial-temporal lobe system is not where memories are permanently stored: this purpose is served by the cortex. Squire and Zola-Morgan (191) propose that memory for an event is distributed across a number of different cortical sites, each representing a different aspect of the event, and that the medial-temporal lobe memory system serves to bind these different sites together, forming a unified representation. The characteristic failure of explicit memory in amnesic patients presumably reflects the lack of this binding function: given a retrieval cue, patients cannot use links (that would have been established by an intact hippocampus) to retrieve associated memories. However, event-related information supported by the several cortical sites is sufficient to support performance on tests of implicit memory.

AWARENESS, MEMORY, AND SURGICAL ANESTHESIA

Prior to the introduction of surgical anesthesia in the 19th century, pain and explicit memory of it were considered a normal part of the surgical procedure (158). Although extensive efforts were made to alleviate pain with hypnosis, ingestion of alcohol, herbs, botanical extracts, and the local application of pressure or ice on nerves, surgery was generally a painful and memorable experience. It is interesting that in South America the Incan priests were quite successful at pain relief for trephination simply by allowing cocaine-saturated saliva to drip into the wound. Still, one might expect that those who underwent this procedure were aware of it at the time and remembered it later.

The distinction between awareness and memory was made very early in the history of the practice of surgical anesthesia. In January 1845, Horace Wells attempted the first public demonstration of nitrous oxide as a general anesthetic. The patient, undergoing removal of an impacted tooth, screamed and struggled throughout the procedure, and Wells was jeered by the audience. Despite this apparent failure of anesthesia, the patient later claimed to have no memory for the procedure. Thus, the patient was aware of the procedure, and in obvious pain during it, but remembered nothing of it later. This is in contrast to the first public demonstration of ether by William Morton in 1846. Morton anesthetized Edward Gilbert Abbott, a young printer, for the surgical repair of a congenital venous malformation in his left cervical triangle. The demonstration was a success: the patient showed no obvious evidence of awareness or pain during the procedure, and no memory of pain afterwards.

The subsequent development of the clinical practice of anesthesia was haunted by the risk of inadequate depth, resulting in awareness and/or recall (for a review of the assessment of anesthetic depth, see ref. 199). Moreover, this risk underwent an abrupt increase when neuromuscular blocking agents were introduced into the practice of anesthesia in the 1940s (98). These drugs made lighter planes of anesthesia possible, thus decreasing the risk of morbidity. However, as Cherkin and Harroun (50,99) and Crile (63) warned, they effectively prevented inadequately anesthetized patients from communicating their awareness to the anesthesiologist, and obtaining relief. Thus, the muscle relaxants effectively increased the risk of surgical awareness.

Incidence of Surgical Awareness

The incidence of surgical awareness is thankfully low: the highest incidence reported is 2–4% and this under very light planes of anesthesia (4,40,41,62,178,208). Hutchinson (104) reported only 1.2% incidence of any sort of recall; Faithfull (83) recorded only five instances of postoperative recall in a series of 1,328 surgical patients; Wilson et al. (215) estimated an incidence of 1%; Moerman and Porcelijn (148) reported only two such incidents among 557 patients who had undergone a total of 1,000 surgical procedures, and Liu et al. (136) gave an estimate of 0.2%. However, Winterbottom's (219) classic case does have its contemporary counterparts: Tracy (200) has provided an especially vivid example from her own experience as a patient. Of course, not all cases of awareness and memory can be attributed to improperly administered anesthetic. Awareness is especially common in situations where relatively light planes of anesthesia are the standard of care: caesarian sections, trauma surgery, and cardiopulmonary bypass surgery. Even the possibility of intraoperative awareness and postoperative memory can cause preoperative anxiety. Cases where awareness and memory occur unexpectedly can result in posttraumatic stress disorder for the patient, and a lawsuit for the practitioner.

During postoperative interviews, patients are frequently surprised to learn that during their stay in the postanesthesia care unit, immediately after surgery, they were alert and talkative, sometimes carrying on long conversations with the staff. They were certainly aware of themselves and their surroundings at the time, but they no longer remember this episode in their lives.

Anesthesiologists have often wondered if their patients were in fact aware during surgery, even though they do not remember their awareness later (a question somewhat analogous to whether a tree falling in a forest makes a sound if no one hears it). One way of approaching this question is through the isolated forearm technique, in which an arm tourniquet is applied prior to administration of neuromuscular blockers. With a prearranged hand-signal, the patient is able to communicate if he or she is aware. This technique was introduced by Tunstall (207) as an aid to assessing anesthetic depth during caesarian sections (see also ref. 39). A recent study of this procedure, involving 30 patients (128), yielded some disturbing findings: at the time of skin incision, 97% of patients signaled awareness and pain; this figure dropped to 77% for awareness and 63% for pain 1 min later, and 20% for awareness and 7% for pain 2 min later; one patient remained aware at 3 min. During postoperative interviews, none of the patients remembered experiencing any pain, or making any signals. Apparently, the tree falling does, indeed, make a sound.

IMPLICIT MEMORY AFTER GENERAL ANESTHESIA

For the first 100 years of general anesthesia, physicians and patients were primarily concerned with whether the technique worked as advertised to prevent concurrent and retrospective awareness of surgical events. The idea that memory for intraoperative events might be preserved outside awareness came only later. Apparently Cheek (46–48) was the first to seriously raise this possibility. Cheek studied a group of patients with poor postsurgical outcome. None of the patients had any explicit memory of surgical events. But when hypnotized, many of them were able to remember negative statements that had been made about them, during surgery, by members of the surgical team. Cheek suggested that these memories unconsciously influenced the patients' postoperative course.

Other clinicians have made similar observations (for example, see refs. 81,82), although the patients' reported memories are not always easy to verify. Goldmann et al. (93) elicited memories of intraoperative events from seven of 33 patients, sometimes with the aid of hypnosis, but only three of these memories were corroborated by the operating room records.

At about the same time, Levinson (130) reported a case of a woman who suffered from a severe depression after plastic surgery on her face. When interviewed under hypnosis, she repeated the words of her surgeon, describing what he thought was a malignant tumor inside her mouth. Because the mass proved benign, the episode was never mentioned to the patient postoperatively. Nevertheless, Levinson (130) concluded that the patient had learned of the possibility of cancer during her surgery, and that this knowledge had unconsciously affected her postoperative mood. This case directly motivated one of most notorious studies in the history of medicine (131). (For other accounts of this study and its context, see refs. 132,133.) By prior arrangement with the surgeon, Levinson (130) staged a mock surgical crisis for each of 10 patients. The patients were anesthetized with a combination of nitrous oxide, oxygen, and ether (there was no muscle relaxant). At a particular point, the anesthesiologist stopped the operation, and announced that the patient had turned blue and might die; shortly thereafter, the anesthesiologist declared that the patient was out of danger and permitted the surgery to proceed. None of the patients had any conscious recollection of this episode. One month later, however, when hypnotized and age-regressed to the time of the surgery, four patients repeated the words of the anesthesiologist verbatim, while four more reported that something bad had happened but they did not know what it was. The remaining two patients recalled nothing at all. Although there is no evidence that the patients' postoperative course was influenced by the mock crisis, the results of the hypnotic interviews indicated to Levinson (130) that the event had been processed and maintained in memory, albeit outside of awareness.

Cheek's and Levinson's reports languished in the literature for two decades. In a review of anesthetic awareness and memory, Trustman et al. (201) concluded that anesthetized patients processed surgical events to the extent that they were awake—an echo of the famous conclusion of Simon and Emmons (185) about the possibility of sleep learning (for updates, see refs. 1,73). There the matter probably would have rested, had it not been for two factors: the conviction of some physicians and psychologists that some degree of information-processing, if not frank awareness, continued during anesthesia; and mounting evidence of spared implicit memory in brain-damaged patients and others who were densely amnesic on tests of explicit memory. The current revival of interest in awareness and memory in anesthesia may be traced to this fortuitous combination of clinical concern and experimental results.

Intraoperative Instructions for Postsurgical Behavior

Credit for rekindling the question of surgical awareness and postsurgical memory goes to Bennett (21; also see refs. 15–18,20). Bennett (21) instructed anesthetized patients that, when interviewed postsurgically, they should pull on their ears to indicate that they had heard his message during surgery. Compared to control patients who heard only operating room conversation through their earphones, a significant number of patients in the experimental group displayed the instructed behavior, even though none of them had any conscious recollection of the contents of the tape (thus, they did not appreciate the significance of their behavior, or experience it as an intentional act). Moreover, patients in the experimental group spent more time touching their ears than those in the control group. These findings were substantially replicated in a subsequent study, which compared four different motor behaviors, only one of which had been targeted by the instructions (22; see also ref. 18). Similar results were obtained by Goldmann et al. (93). These investigators were unsuccessful in inducing patients to pull on their ears, although they were successful when patients were instructed to touch their chins! Although Merikle and Rondi (143) have raised questions about the statistical analysis of this study, Block et al. (26) also obtained an instructed motor effect. Their study compared two behaviors: one targeted by the intraoperative instruction and the other never mentioned intraoperatively.

However, not all attempts to replicate Bennett's findings have been successful. Jansen et al. (109) failed to find any difference in instructed ear touching between experimental and control groups in a study which followed a standard anesthetic protocol involving enflurane, and included pre- and postoperative testing of the target behavior. Three other studies also found no evidence of the behavior suggested during surgery (23,24,140). Finally, two studies in which Bennett himself was a co-investigator found no difference between experimental and control conditions (51,69); a third study found the effect under nitrous oxide but not under isoflurane (68).

In principle, positive response to intraoperative instructions fits the formal definition of implicit memory: a change in experience, thought, or action (e.g., ear-touching behavior) that is attributable to a past event (delivery of the instruction) in the absence of conscious recollection of that event. Bennett's initial study (21) helped set the stage for subsequent work on implicit memory, but it has also been criticized on methodological grounds (144,214; for a reply, see ref. 17). For example, the statistical significance of the instruction effect may have been carried by two patients who showed extraordinarily high levels of ear touching; when these two subjects are eliminated, there is no difference between the experimental and control subjects. This problem confronts the study of Block et al. (26) as well as Ghoneim and Block (88), although, apparently, the overall effect was not entirely carried by a few outliers. In addition, Merikle and Rondi (143) have raised questions about Goldmann et al.'s (93) statistical analysis. At present, then, the suggestion that patients can respond postoperatively to intraoperative instruction for motor behavior remains a tantalizing possibility, but one which has not received adequate experimental support to date.

FORMAL STUDIES OF IMPLICIT MEMORY FOLLOWING GENERAL ANESTHESIA

Recent years have seen an explosion of studies employing more conventional implicit-memory paradigms of a sort familiar in cognitive psychology. In these experiments, adequately anesthetized patients are presented with auditory stimulus material, and then complete postoperative tests of explicit and implicit memory. The goal of these studies has been to search for functional dissociations between explicit and implicit memory analogous to those observed in cases of amnesia. The general hypothesis of this research is that while explicit memory for intraoperative events (recall and recognition) is grossly impaired (as indeed it should be) under at least some conditions of adequate anesthesia implicit memory (such as priming) will be spared.

Priming Effects

By far, the greatest portion of the literature on implicit memory following anesthesia involves priming effects of one sort or another. That is, the investigators seek evidence of improved performance on some perceptual-cognitive task that is attributable to the patient's surgical experience, in the absence of conscious recollection of that experience. In most of these experiments, performance on some priming test of implicit memory is compared with a free recall or recognition test of explicit memory.

The first experiment of this type yielded negative results. Eich et al. (74) presented anesthetized patients with a tape recorded list of items consisting of a homophone (e.g., ATE or EIGHT, PIECE or PEACE) and a disambiguating context (e.g., Dinner at EIGHT; War and PEACE). Ordinarily, such an experience will bias the subject's spelling of these words on a later test, regardless of whether the list items themselves are remembered—clear evidence of priming, and thus of implicit memory. Among patients who heard the tape preoperatively, Eich et al. (74) obtained the expected priming effect on spelling performance. When the tape was presented intraoperatively, however, they found no evidence of either explicit or implicit memory.

In contrast, the next study yielded positive results. Kihlstrom et al. (127) prepared two lists of paired-associates of the form OCEAN-WATER; one of these was presented to patients anesthetized with isoflurane, and the second list, carefully matched to the first in terms of normative cue-target probability, served as a control. Anesthesia was induced by thiopental and maintained with isoflurane, and the critical tape was played from the first incision to the last stitch. On an initial interview in the recovery room, the patients remembered nothing of the list. The left-hand panel of Fig. 2 shows the results of explicit and implicit memory testing. For the explicit memory test, the patients were presented with the cue terms from both lists of paired-associates and asked to recall the response term with which each cue had been paired. Obviously, this is possible only for the list actually presented for study. Nevertheless, there was no difference in the proportion of targets recalled from the critical and neutral list. For the implicit memory test, the subjects were presented with the cues and asked simply to respond with the first word that came to mind. Here, the patients showed a significant priming effect: they were more likely to produce targets as free associates to critical than neutral cues. Taken together, these results indicate that while the patients had no explicit memory for items presented during surgery, implicit memory for these items was preserved to some degree. (The order of explicit and implicit tests was counterbalanced across subjects, and there was greater priming observed when free association preceded cued recall.)

In a subsequent experiment, Cork et al. (55) repeated this procedure with patients whose anesthesia was maintained by sufentanil and nitrous oxide in oxygen (for a direct comparison of the two experiments, see ref. 56). In order to examine implicit memory in the absence of explicit memory, a few patients who showed some recall of intraoperative events on an initial interview were excluded from further consideration. The right-hand panel of Fig. 2 shows the results of cued recall and free association memory testing in the remaining patients. In

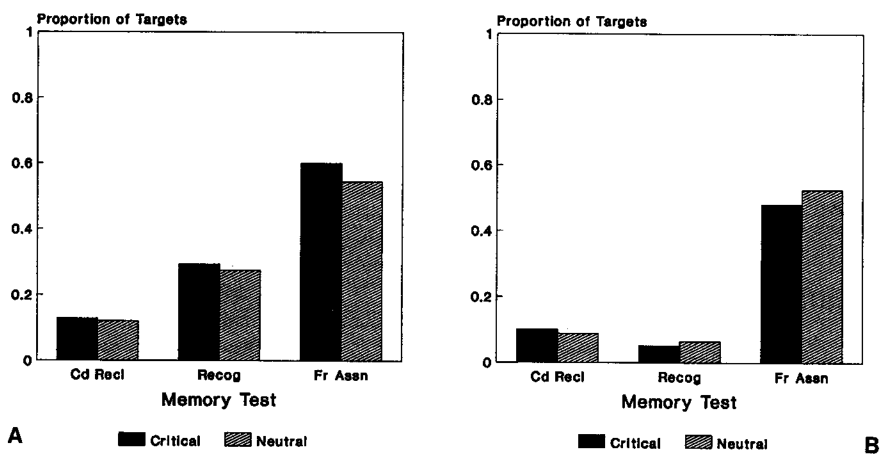

Figure 2. Performance on explicit and implicit memory tests following general anesthesia with isoflurane (127) (**A**) and sufentanil/nitrous oxide (55) (**B**). Cd Recl, cued recall; Recog, recognition; Fr Assn, free association.

this experiment, there was evidence of neither explicit nor implicit memory, regardless of the order of testing. Thus, explicit and implicit memory were dissociated with isoflurane anesthesia, but not with sufentanil/nitrous oxide.

A similar pattern of results had been obtained earlier in a pair of studies reported by Couture et al. (59; see also refs. 196,197). In the first study (196), surgical patients were randomized to one of two groups. Anesthesia was induced with thiopental and maintained with isoflurane. During surgery, patients in the experimental group heard a list of six low-frequency words (e.g., CORUSCATE, TERGIVERSATION) repeated a total of 19 times; controls heard a list of six pseudowords. Within 48 h of their operation, the patients were asked to listen to a tape recording of 36 words, including the six words presented to the experimental group, and to circle on a list any words which seemed familiar. Figure 3 shows the results. The patients in the experimental group were much more likely than their counterparts in the control group to identify the six target words as familiar, even though they had no memory that any of the words had been presented during surgery. The effect of exposure on familiarity judgments is a priming effect indicative of implicit memory. Still, a subsequent experiment (197), in which anesthesia was induced by thiopental but maintained with fentanyl and nitrous oxide in oxygen, showed no difference between experimental and control groups. The results are also presented in Fig. 3. Thus, as in the studies by Cork et al. (54–56), explicit and implicit memory were dissociated with an inhalant anesthetic but not with an opioid derivative.

Following on these studies, a large number of investigations have compared postsurgical explicit and implicit memory in patients receiving general anesthesia. These experiments have employed a wide variety of paradigms, and they have produced a mix of positive and negative results (see also refs. 8,9,19,52,88,89,121,143).

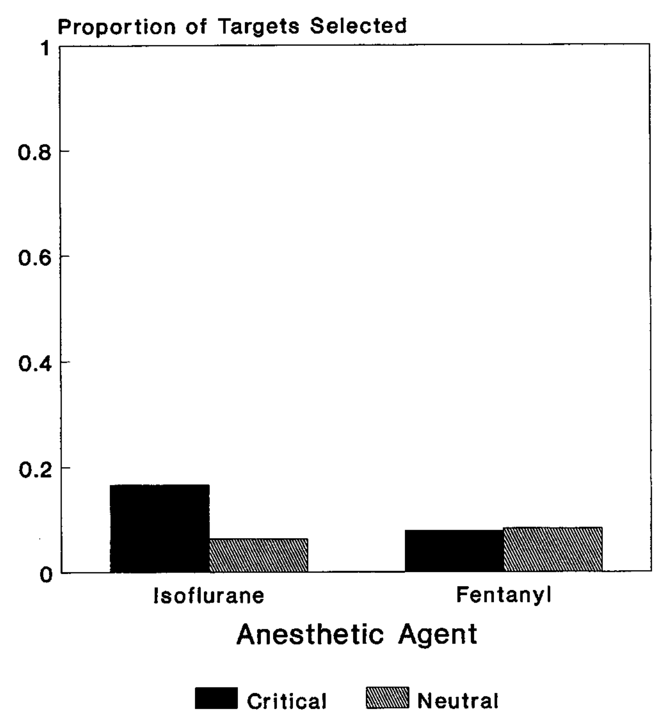

Figure 3. Performance on familiarity judgments following general anesthesia with isoflurane and sufentanil/nitrous oxide. (Reprinted, in adapted form, with permission from Couture LJ, Stolzy, SL, Edmonds HL. Postoperative evidence of intraoperative implicit perception of words: a comparison of two anesthetic techniques (submitted)

Homophone Spelling

Using the homophone-spelling paradigm employed by Eich et al. (74), Westmoreland et al. (213) also failed to obtain evidence of implicit memory.

Free Association

Humphreys et al. (102) combined the free-association and homophone-spelling paradigms. They presented homophones in a disambiguating context, as Eich et al. (74) had done. Instead of asking subjects to spell the homophones, however, they collected free associations to the ambiguous words. Scoring of these associations indicated that they were influenced by the context in which the cues had been presented during surgery. This effect held only for items presented at a very light plane of anesthesia (<1.2% end-tidal concentrations of isoflurane); although it should be understood that the patients were adequately anesthetized throughout the procedure.

Employing a more conventional free-association procedure, Bethune et al. (23) presented their patients with target words and sentences of the form, "Tar makes a mark," at the rate of 20 times/h during surgery. Later, subjects were presented with the sentences frames, and asked to report the first word which came to mind. Subjects whose anesthesia was induced with fentanyl and maintained with propofol produced more list items than those who received fentanyl followed by methohexitone.

Schwender et al. (177) employed fentanyl in combination with benzodiazepine, isoflurane, or propofol, in three separate groups of ten patients. During surgery, the patients were read the Robinson Crusoe story; 3–5 days later, they were asked to free-associate to the word "Friday." Half the patients in the benzodiazepine group responded with "Robinson Crusoe," whereas only one in each of the other groups did so (in a control group which did not hear the tape, none responded with "Robinson Crusoe9). Interestingly, these investigators also monitored the mid-latency auditory event-related potential (MLAERP), an EEG component that occurs 20–100 ms after auditory stimulation. The MLAERP was preserved in the benzodiazepine group, but suppressed in the isoflurane and propofol groups. (In the studies reviewed in this chapter, spared implicit memory provides indirect evidence of cognitive processing during anesthesia. The ERP, whether elicited by auditory or tactile stimulation, provides such evidence directly; see refs. 120,126. For example, evidence that the middle or, especially, late components of the ERP are preserved would indicate that anesthetized patients are performing rather complex cognitive operations on environmental stimuli, regardless of whether these events are subsequently remembered; for reviews of this research, see refs. 159,176,194,198,199.)

Category Generation

A variant on free association is category generation, in which subjects are asked to give instances of taxonomic categories such as ARTICLE OF CLOTHING or FOUR-FOOTED ANIMAL. In the first study of this type, Roorda-Hrdlickova et al. (168) presented the words YELLOW BANANA, GREEN PEAR during surgery under nitrous oxide and isoflurane; later, the patients were asked to generate instances of the categories VEGETABLES, FRUIT, AND COLORS. In this study, patients who heard the list during surgery were more likely to produce target items than were those who heard a tape of neutral sounds. These findings were replicated by Jelicic et al. (112), employing nitrous oxide and fentanyl or sufentanil as the anesthetic agent. Evidence of priming was also obtained by Brown et al. (42). In this case, however, the evidence was of negative priming: target items were significantly less likely than neutral items to be produced as category instances.

Despite these positive results, other investigations have failed to obtain evidence of priming on category-generation tasks (10,26,29,45,52,192,209,213).

Perceptual Identification

A common finding in the priming literature is that previously presented words are more readily identified under conditions of degraded input, such as brief visual presentation, or following a printed word with a pattern mask (for example, see ref. 105). Charlton et al. (45) employed such a task, in which critical and neutral items were presented auditorily against a background of white noise. The patients were more likely to identify critical than neutral items. However, when these words were presented clearly to subjects for an explicit recognition task, subjects were unable to distinguish critical from neutral items. Thus, implicit memory as represented by the lexical identification task was dissociated from explicit memory as represented by the recognition task.

Stem Completion

Another popular task in the implicit-memory literature is word-stem completion. Block et al. (26) found a small effect evidence of priming on this task, but the anesthetized patients' initial exposure to the words was necessarily auditory, while the test was presented visually. This is a problem because implicit memory is often modality specific—i.e., that implicit memory is preserved only when the modality of test matches the modality of study (for example, see ref. 105). Therefore, a shift in modality between presentation and test might have depressed any effect. Recently, Bonebakker et al. (30) carried out a similar study with an auditory stem-completion test, and obtained a significant priming effect. This kind of study requires pronounceable word stems; for this reason, a study of word-fragment completion following auditory presentation of whole words is probably impossible.

Affective Judgments

A few researchers have sought evidence of postoperative implicit memory in the mere exposure effect, by which exposure to an item increases a subject's preference for that item (222). As noted earlier, the mere exposure effect occurs with subliminal as well as supraliminal stimulus presentation (34), raising the possibility that it might occur for stimuli processed during anesthesia as well. So far, four studies have been performed, yielding conflicting results. (Insofar as the affective judgments are mediated by exposure, the familiarity-rating task employed by Couture et al. may be another instance of this genre; for this work, see ref. 59.) Block et al. (26) did find a marginal increase in preferences for pseudowords presented during anesthesia. Items which had been presented 16 times were preferred over those which had been played 0–8 times. On the other hand, Winograd et al. (217) played a tape recording of unfamiliar melodies (actually, non-Western folk music) three times to patients anesthetized with a combination of nitrous oxide and oxygen, isoflurane, and sufentanil. On postoperative testing, there was no evidence of a mere exposure effect; by contrast, melodies which had been played three or 12 times to a control group were preferred over those which had not been played previously. Caseley-Rondi et al. (44), in a study involving preference for Japanese melodies played eight times, also failed to find an exposure effect. In a study of children, Bonke et al. (33) played a tape consisting of 20 repetitions of the sentence THE CHILD IS PLAYING WITH THE __ BALL, with the blank filled in with the color orange or green. Later, when the children were given an opportunity to color a picture of a ball, their color selections were unrelated to the tape which had been played.

A variant on the mere exposure paradigm is the "false fame effect" discovered by Jacoby et al. (106,108). These investigators found that presentation of an unfamiliar name increases the likelihood that this name will be judged famous on a subsequent test; apparently, the misattribution of fame is mediated by priming effects, and a feeling of familiarity, similar to those observed in the mere exposure paradigm. Interestingly, the false fame effect is independent of subjects' ability to remember the names which they had studied; and amnesic patients show the effect even though they cannot remember the study trial (190). Thus, misattributions of fame constitute evidence of implicit memory. Jelicic et al. (113) obtained a false fame effect for names presented to anesthetized patients, but they failed to replicate themselves in a subsequent experiment (110).

Fact Learning

Another line of research bearing on the question of preserved implicit memory comes from experiments in which patients are presented with obscure "trivia" information during surgery. Of course, adequately anesthetized patients will have no memory for the learning experience itself. However, studies of other forms of amnesia have indicated that patients and subjects can acquire new semantic knowledge, even if they do not remember the episode in which that knowledge is acquired—a phenomenon termed source amnesia (80,174,184). Source amnesia reflects implicit memory because it is a change in behavior—the ability to answer certain factual questions—attributable to a past experience (e.g., hearing the answers to these questions over an audiotape) in the absence of conscious recollection of the learning experience.

A study informally reported by Goldmann (92) was the first to demonstrate source amnesia following adequate anesthesia. During surgery, the patients were played a tape containing a number of trivia questions and their answers (e.g., "What is the blood pressure of an octopus?). The patients' knowledge of these answers (tested by recognition) improved from pretest to posttest, although few if any of the patients had awareness that they had been taught the answers during surgery. More recent attempts to replicate this finding have yielded mixed results (68,69,110,113).

Conditioning

In classical (or Pavlovian) conditioning, the repeated pairing of a stimulus (the unconditioned stimulus, US) which routinely elicits a reflexive response (the unconditioned response, UR) with a neutral stimulus (the conditioned stimulus) leads to the appearance of a new response (the conditioned response, CR) to the CS which resembles the UR. Classical conditioning is ubiquitous, in that it can be observed in some form in almost every species with a nervous system (163). Of course, experiments on nonhuman animals clearly show that CRs can be acquired during anesthesia, and preserved after recovery, so long as the URs can be elicited by the USs. Because, in strictly logical terms, an organism need not consciously recollect the acquisition trials in order to give CRs to CSs, conditioning counts as an expression of implicit memory. Ghoneim et al. (90) failed to obtain evidence of classical conditioning in patients anesthetized with isoflurane and nitrous oxide, but this may have occurred because the anesthetic agents prevented the US from eliciting the UR in the first place.

Recognition Memory Redux

By definition, adequate general anesthesia renders a patient unable to consciously remember surgery. This assumption is confirmed by a number of experimental studies which fail to find evidence of either recall or recognition of intraoperative events (for example, see refs. 55,74,127,137,155,209). This is so even when recollection is attempted while the patient is hypnotized (18,21,93). The recognition results are especially reassuring, because recognition is generally considered to be a very sensitive test of explicit memory.

It is important to note, however, that most studies of recognition after anesthesia have used a yes/no procedure, in which subjects were asked to examine test items, including both targets and lures, and to indicate whether each had been presented previously. In another type of recognition test, known as forced-choice, subjects are presented with pairs (or larger sets) of items, one critical and one or more neutral, and required to select the one which had been previously presented—guessing if necessary. Employing such a test, Dubovsky and Trustman (67) found no evidence of recognition; Block et al. (26) obtained evidence of recognition for nonsense syllables, but not words, presented during surgery. Actually, however, there are reasons to think that forced-choice recognition might be spared, to at least some degree, if implicit memory is also spared. Mandler (139) has argued that recognition is a judgment of prior occurrence which can be made on the basis of two sorts of information: (a) a feeling of familiarity, such as occurs when a name or face "rings a bell," or (b) retrieval of the circumstances under which we previously encountered the object or person. From Mandler's (139) point of view, the "bell-ringing" recognition by familiarity is mediated by the same activation of prior knowledge which (according to his view) mediates priming. Forced to choose, subjects strategically rely on perceptual salience, or other phenomenal qualities which accompany priming effects, to construct inferences, or make informed guesses, about study items which are right more often then they are wrong. It should be understood, however, that priming-based recognition by familiarity does not compromise the postoperative amnesia which is part and parcel of the definition of adequate anesthesia. This is because the recognition is largely inferential; unless they are forced to choose or encouraged to guess, adequately anesthetized patients will rarely if ever recognize intraoperative events as such.

In fact, Bonebakker et al. (30) have obtained evidence of forced-choice recognition (explicit memory) as well as priming in word-stem completion (implicit memory). In accounting for this result, it is important to note that the procedure employed by these investigators differed from its predecessors in important respects. They presented the patients with two lists of words, one preoperatively and one intraoperatively; after surgery, the patients were tested on both lists. Recognition for a list of words presented intraoperatively was grossly impaired compared to recognition of a list presented preoperatively, but for the intraoperative list there were significantly more hits than false alarms. Anesthesia has no retrograde effect on memory, so it is not surprising that the patients were able to recognize some items from the preoperative list; this, in turn, may have created a mental set in which they were able to make better-than-chance recognition judgments about items from the intraoperative list. Similarly, in studies discussed below, Evans and Richardson (78) and Casely-Rondi et al. (44) found that, forced to choose, patients could guess with above-chance accuracy which of two tapes had been played to them during surgery; however, Bethune et al. (24) did not get this effect. Earlier, Millar and Watkinson (145), employing a signal-detection procedure in which patients were encouraged to guess, found significant yes/no recognition of words presented during surgery. (For a discussion of this experiment and its implications for implicit memory, see ref. 126.)

It would be interesting to know whether the patients could distinguish between the two sets of items; perhaps they incorrectly attributed items from the intraoperative list to the preoperative list. In any event, the above-chance levels of forced-choice recognition does not imply that the patients were inadequately anesthetized; rather, it suggests that the preserved implicit memory indicated by the stem-completion test served as the basis for "informed guessing"—the recognition-by-familiarity of Mandler (139)—on the recognition test.

EFFECTS OF INTRAOPERATIVE THERAPEUTIC SUGGESTIONS

Some practitioners, apparently inspired by the positive evidence of intraoperative information processing, or at least convinced of its possibility, have suggested that therapeutic suggestions, analogous to those administered in hypnosis, might be effective in relieving postsurgical pain and improving postoperative recovery. Following some uncontrolled clinical observations of therapeutic suggestion, Pearson (157) was the first to attempt a controlled, double-blind study. He found that patients who received therapeutic suggestions during surgery were discharged sooner than those who were played only music or a blank tape. However, the two groups did not differ in terms of their need for postoperative narcotic analgesia or rated course of recovery. Although no memory tests of any kind were administered in Pearson's study, the effects on postoperative release fit the formal definition of implicit memory: a change in experience, thought, or action that is attributable to some past event, independent of conscious recollection of that event.

The findings of Pearson's (157) pioneering study have been supported in some, but not all, subsequent investigations (for example, see refs. 2,24,25,28,32,44,58,78,79,85,86,111,135, 140, 151,195,220,221). Evaluation of this body of literature is made difficult by the wide variety of surgical procedures, anesthetic agents, and outcome measures employed (8,44,143). Moreover, many studies employ multiple measures of outcome, not all of which yield the same results; because multiple measures can capitalize on chance, interpretation of these studies is ambiguous.

Still, some of the findings in this literature are extremely provocative. For example, in a double-blind study of patients receiving total abdominal hysterectomy, Evans and Richardson (78) found that patients who heard a tape containing suggestions for postoperative comfort, lack of pain and nausea, etc., were discharged from the hospital an average of 1 day earlier than those who heard a blank control tape. They also showed less pyrexia and less difficulty with their bowels. Bethune et al. (24), studying angina patients receiving elective coronary artery bypass surgery, found a difference of 2 days in duration of hospital stay. McClintock et al. (140) placed a group of hysterectomy patients on patient-controlled analgesia (PCA); those who were played a tape of therapeutic suggestions during their surgery showed a 23% reduction in morphine consumption over the next 24 h. Steinberg et al. (195) obtained similar results in a study of patients undergoing hysterectomy or breast reconstruction. Caseley-Rondi et al. (44) also obtained a significant effect on PCA, in a study of patients receiving hysterectomy or oophorectomy. This study is especially significant for its introduction of a novel control group: some patients heard suggestions, while others heard soothing melodies; others heard both, while the rest heard neither. The discharge and PCA effects are particularly interesting, because they are behavioral in nature, and thus not vulnerable to the criticisms often directed at self-reports.

With respect to memory and recall, the positive effects of intraoperative therapeutic suggestion are of interest because they fit the formal definition of implicit memory: an effect of a past event on subsequent experience, thought, and action, independent of conscious awareness of that event. Positive results clearly indicate that information from the tape was encoded and stored in memory. It should be understood, however, that negative results are equivocal with respect to implicit memory. This is because positive response requires that the suggestion be both processed and executed. Consider an analogy to hypnosis: positive response to hypnotic suggestions obviously indicates that the subject has heard them; but negative response may be due merely to the fact that the subject lacks the degree of hypnotizability needed to respond positively. Similarly, intraoperative therapeutic suggestions may be encoded in memory, but remain unexpressed because the patient lacks the capacity to execute them. Intraoperative therapeutic suggestions are modeled on hypnotic suggestions, and it has sometimes been suggested that hypnotizability might mediate their outcomes. Although hypnotizability does seem to mediate the somatic outcomes of hypnotic suggestion (37,38), Casely-Rondi et al. (44) found no such effect for intraoperative suggestion. Studies of therapeutic suggestions which yield null results should not count as evidence against implicit memory following general anesthesia.

CONSCIOUS SEDATION

In cases where awareness is possible or cannot be prevented, as in trauma surgery or the modern practice of conscious sedation, administration of benzodiazepines can result in an anterograde amnesia for surgical events (91,153,160). However, it should be understood that the anterograde amnesia covers only explicit expressions of memory. Implicit memory is relatively spared by benzodiazepines (this is also the case for nitrous oxide) (27). In a study by Fang et al. (84), volunteer subjects (not surgical patients) who had heard a list of words while sedated with diazepam performed more poorly on a test of free recall (explicit memory) than control subjects who were not drugged. On a second test, the subjects were presented with three-letter stems that could be completed by list items. Subjects in the two groups were equally likely to produce list items on this test of implicit memory. Similar findings were obtained by Danion et al. (66), although exactly the reverse—explicit memory spared, implicit memory impaired—were obtained in a study reported by Danion et al. (65). A series of studies by Polster et al. (161,162) also documented dissociations between explicit and implicit memory produced by midazolam and propofol.

The sparing of implicit memory under propofol was recently confirmed by Cork et al. (54) in the first study of memory following conscious sedation to involve actual patients rather than volunteer subjects. Patients scheduled for ambulatory surgery received an intravenous bolus of propofol and fentanyl prior to surgery; during the operation, propofol was constantly infused, with supplemental boluses under the control of either the anesthesiologist or the patients themselves. At the last skin stitch, an audiotape presented a list of 15 paired associates of the sort employed by Kihlstrom et al. (127) and Cork et al. (55). After 1 h in the recovery area, the patients completed a series of free recall, free association, cued recall, and recognition tests for the critical and neutral lists (those patients showing any free recall were removed from subsequent analyses). Figure 4 shows that on tests of cued recall and recognition there was no advantage for the critical over the neutral list; that is, the patients had essentially no explicit memory for the items which they had studied during surgery. In the free association test, however, they were much more likely to give the targeted response to cues from the critical list than to cues from the control list; in other words, the patients showed significant priming on this test, indicating that implicit memory had been preserved to some degree.

In general anesthesia, adequately anesthetized patients lack both concurrent and retrospective awareness of surgery: they are not cognizant of these events as they occur, and they have no memory of them afterward. Conscious sedation separates these two functions: the patient is aware of what is happening, but has no memory afterwards. Apparently, sedative drugs prevent adequate encoding of surgical experiences, leading to a failure of explicit memory. However, implicit memory is largely independent of elaborative and organizational activity at the time of

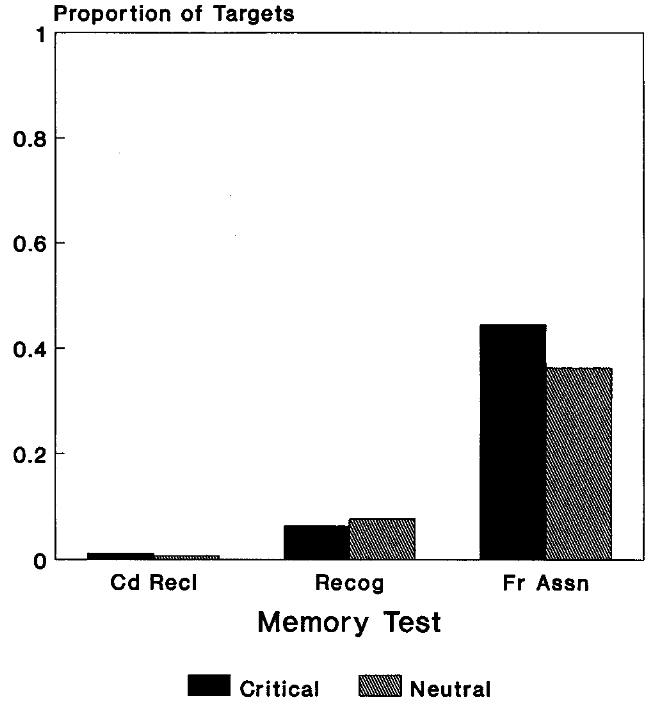

Figure 4. Performance on explicit and implicit memory tests following conscious sedation with propofol (54). Cd Recl, cued recall; Recog, recognition; Fr Assn, free association. (Reprinted, in adapted form, with permission from Cork RC, Friley KA, Heaton JF, Campbell CE, Kihlstrom JF. Effect of sedation with propofol on implicit memory (submitted).

encoding. The sparing of implicit memory has obvious implications for the use of benzodiazepines and other agents to control memory in both conscious sedation and general anesthesia. Although administration of sedatives may produce a dense amnesia in terms of conscious recollection, surgical events may nonetheless influence the patient's postsurgical experience, thought, and action outside of phenomenal awareness.

There have been no studies of the effect of therapeutic suggestions administered during conscious sedation. In view of mounting evidence that preoperative psychosocial interventions can facilitate recovery from surgery (for example, see ref. 150), experiments with therapeutic suggestions administered during conscious sedation would seem to be in order.

FACTORS AFFECTING IMPLICIT MEMORY AFTER GENERAL ANESTHESIA

Table 1 summarizes the results of those formal studies of implicit memory, published through the end of 1994, which have employed standard laboratory tasks. The studies of therapeutic suggestion have been excluded, because (for reasons noted above) negative results are ambiguous with respect to the question of implicit memory. Scientific understanding is advanced by producing an effect reliably; it can also be advanced by making it go away reliably. Thus, the mix of positive and negative results reviewed displayed in this table is not disconcerting, provided that some pattern is discernable. Unfortunately, no such pattern is discernable yet, perhaps because this line of research is in its infancy. For this reason, too, we have not performed a metanalysis of the available literature. Still, some comments may help direct future studies in this area to the point where systematic metaanalyses might be very fruitful.

For example, it is clear that progress in this area can only be made when the patients enrolled in these experiments receive standardized anesthetic regimes. Unless this occurs, positive

Table 1. FORMAL STUDIES OF IMPLICIT MEMORY FOLLOWING GENERAL ANESTHESIA: SUMMARY BY PARADIGM SINCE 1985

Positive results	Negative results
Behavioral response	
Bennett and Boyle, 1986 (20)	McClintock et al., 1990 (140)
Goldmann et al., 1987(93)	Jansen et al., 1991 (109)
Bennett et al., 1988 (22)	Bethune et al., 1992 (23)
Block et al., 1991 (25)	Dwyer et al., 1992 (68)
Dwyer et al., 1992 (68)	Dwyer et al., 1992 (69)
	Bethune et al., 1993 (24)
	Chortkoff et al., 1993 (51)
Homophone spelling	
	Eich et al., 1985 (74)
	Westmoreland et al., 1993 (213)
Free association	
Kihlstrom et al., 1990 (127)	Cork et al., 1992 (55)
Bethune et al., 1992 (23)	
Humphreys et al., 1993 (102)	
Schwender et al., 1994 (177)	
Category generation	
Roorda-Hrdlickova et al., 1990 (168)	Standen et al., 1987 (192)
	Block et al., 1991 (25)
Jelicic et al., 1992 (112)	Bonebakker et al., 1993 (29)
Brown et al., 1992 (42)	Charlton et al., 1993 (45)
	Chortkoff et al., 1993 (51)
	Villemure et al., 1993 (209)
	Westmoreland et al., 1993 (213)
	Andrade et al., 1994 (10)
Perceptual identification	
Charlton et al., 1993 (45)	
Stem completion	
Block et al., 1991 (25)	
Bonebakker et al., 1994 (30)	
Familiarity/fame judgments	
Stolzy et al., 1986 (196)	Stolzy et al., 1987 (197)
Jelicic et al., 1992 (113)	Jelicic et al., 1993 (110)
Affective judgments	
Block et al., 1991 (25)	Winograd et al., 1991 (217)
	Bonke et al., 1993 (33)
	Caseley-Rondi et al., 1994 (44)
Fact learning	
Goldmann, 1987 (92)	Dwyer et al., 1992 (68)
Jelicic et al., 1992 (113)	Dwyer et al., 1992 (69)
	Jelicic et al., 1993 (110)
Conditioning	
	Ghoneim et al., 1992 (90)

effects obtained with one agent (or class of agents) may be obscured by the negative effects of others. Careful control also needs to be exercised over preoperative and postoperative medication. Furthermore, investigators should repeat their experiments across a wide range of anesthetic agents, in order to determine the generalizability of positive (and, for that matter, negative) results. Of course, comparison is made difficult by the task of insuring that patients given different agents are all anesthetized to the same depth; for this reason, further research is also needed to develop techniques for monitoring the depth of anesthesia (116,193). Studies of both patients and volunteers clearly indicate that the effects on memory vary as a function of anesthetic depth (for example, see refs. 10,51,68). However, it should be understood that, in the experiments summarized here, all patients were adequately anesthetized according to standard clinical criteria.

Such comparisons are theoretically important because the amnestic properties of various agents may be related to their biochemical mechanisms of action. The inhalants are nonspecific anesthetics, which apparently act on the neuronal membrane to block the sodium channel; by inhibiting depolarization, they prevent synaptic transmission. By contrast, the opioids, benzodiazepines, and ketamine exert selective blocking effects on the receptors of particular neurotransmitters. In this light, it is interesting that both Couture et al. (59) and Cork et al. (55) found that implicit memory is spared when subjects receive inhalant anesthesia (isoflurane), but not when they receive a nitrous-narcotic preparation (fentanyl or sufentanil). On the other hand, Block et al. (26) obtained evidence of spared implicit memory on one test (stem-completion) under both sorts of conditions, while Schwender et al. (177) found the reverse. Obviously, further research is needed on this topic.

Similarly, careful attention also must be given to the means by which implicit memory is tested. It is easy, and fun, to invent implicit memory tasks. But if research in this area is to progress, it is important to use tasks which have been extensively studied under standard laboratory conditions. Otherwise the investigator risks studying one unknown with another. Unfortunately, many of the best-studied implicit memory tasks (e.g., word-stem- and word-fragment-completion) generally require visual presentation and testing. However, others (e.g., free-association, category generation, homophone-spelling, preference judgments) do not, and some tasks (e.g., perceptual identification and lexical decision) exist in both visual and auditory forms.

Even among these tasks, however, certain characteristics may be critical to the success or failure of the research. For example, the homophone-spelling task requires the subjects to process the meaning of the stimulus word (as implied by its sentence context), and it may well be that such complex cognitive processes are beyond the powers of the anesthetized patient (97,118–121). If patients cannot analyze the meaning of a word at the time of initial presentation, they cannot use semantic information to bias spelling performance at the time of test. There are good reasons for thinking that implicit memory in anesthetized patients, to the extent that it exists at all, is mediated by a perceptual representation system which analyzes the form and structure, but not the meaning, of objects and events (172,175,205).

Accordingly, tests which require subjects to process the semantic properties of stimuli may fail to reveal implicit memory which would be uncovered by tests which require them only to process perceptual properties. In this respect, the successful studies of Kihlstrom et al. (127) and Bethune et al. (23) may seem anomalous, because the priming of free associations would ordinarily seem to require processing of semantic links. However, this is not the case in these studies. In the former study, the whole paired associate, including cue and target, was presented during surgery, as were the targets and their sentence frames in the latter. This is a situation very close to repetition, rather than semantic, priming. Under these circumstances, priming could have been mediated by perceptual rather than semantic representations of the stimuli in question. Other variants on the free-association task, in which the cue and the target were not presented together during surgery, probably would have yielded negative results.

This consideration of the cognitive requirements of different implicit memory tasks is important. Individuals who are unconscious are not able to deploy attention, and engage in complex cognitive activities, such as elaboration and organization, in the way that their conscious counterparts are. Semantic analysis, or at least the elaborative and organizational processing described earlier, appears to be necessary for explicit memory; and the fact that explicit memory is abolished in anesthesia supports the idea that these processes are unavailable to adequately anesthetized patients. However, elaboration, organization, and semantic analysis are not necessary for implicit memory—at least for those forms of implicit memory which are mediated by a perceptual representation system. Thus, implicit memory may well be spared, provided that it is based on a presemantic perceptual representation system. (It should be noted that the involvement of perceptual representations in postoperative implicit memory places limits on the effectiveness of intraoperative therapeutic suggestions, insofar as understanding such suggestions requires semantic processing.) Nevertheless, the sparing of implicit memory, to the extent that it occurs at all, does not mean that the patient was conscious during surgery or was in any sense inadequately anesthetized. Implicit memory in general anesthesia is theoretically interesting precisely because it tests the limits of information-processing outside of conscious awareness and control.

RECOMMENDATIONS FOR CLINICAL PRACTICE

Despite our currently limited knowledge about perioperative awareness and postsurgical implicit memory, there are certain basic, common-sense precautions which clinicians can take to protect patients against explicit memory—and, if intraoperative suggestion actually works, to exploit implicit memory to the patient's advantage.

It has been well documented that preoperative explanation of anesthesia and surgery can take the place of a significant amount of medication in allaying patient fear and anxiety. The anesthesiologist should talk to the patient about the potential for explicit and implicit memory following anesthesia, and offer the patient the opportunity to have something placed over his or her ears during surgery. Alternatives include simple earplugs, designed to take away loud or distracting operating room noises, audiocassette earphones for music that the patient likes, or even positive suggestions recorded by the patient, the anesthesiologist, the surgeon, or anyone else the patient wants. We may not know whether the patient is hearing or will remember anything, but the precautions are so simple and the repercussions for failing to take them so unsavory that it would make sense to provide something for the patient's ears.

In the holding area and prior to the induction of anesthesia, the patient may be in a very terrified state, and the sound environment is important to proper management. Instruments crashing, radios playing, and surgeons conducting detailed conversations about the patient's pathology should be stopped. Again, earphones with taped music or suggestions should be an option.

During anesthesia, derogatory remarks about the patient, as well as negative comments about pathology, should be forbidden. Of course, we do not know that music or taped suggestions improve outcome, but they may keep patients from hearing partial or inadvertent comments. If you do not provide the patient with cassette players and earphones, at least provide earplugs.

The same rules apply to emergence and recovery. Environmental noise and conversation should be controlled. Be prepared to repeat, the next day, postoperative conversations held immediately after the surgery: the patient is likely not to remember them. If the patient is an outpatient, make sure that any explanations or instructions are carefully given to whomever is responsible for taking the patient home.

Admittedly, these are aggressive measures to take to prevent a problem that may never occur. We recommend them, however, because they are easy to accomplish and help protect both the patient and the physician from an unhappy experience. They do no harm, and they may well do some good.

Acknowledgment: Preparation of this paper was supported in part by a grant from the McDonnell-Pew Cognitive Neuroscience Program to the University of Arizona, and by Grant MH-35856 from the National Institute of Mental Health to John F. Kihlstrom. We thank Melissa Birren, Michael Cyphers, Jennifer Dorfman, Elizabeth Glisky, Martha Glisky, Heather Law, Victor Shames, Michael Valdisseri, Susan Valdisseri, and Michele Wright for their comments.

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