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Awareness and information processing in general anesthesia

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Although general anesthesia produces an apparent loss of consciousness, there is some reason to believe that, at least under some circumstances, surgical events may influence post-operative experience, thoughts and action as implicit memories. This paper summarizes a number of recent experiments in which adequately anesthetized patients show implicit, but not explicit, memory for surgical events. The evidence for implicit memory following general anesthesia is mixed, and the limiting conditions are not yet known. Practical and theoretical implications of these findings are explored.

Key words: general anesthesia; memory; surgery; awareness; information processing

Introduction

General anesthesia operates directly on the central nervous system, producing what appears to be a general loss of consciousness that affects sensory awareness in all modalities and at all bodily loci. In typical clinical practice the patient is pre-medicated with a sedative (i.e. a benzodiazepine such as diazepam), which relieves pre-operative anxiety and facilitates the induction of anesthesia. Then the patient receives the intravenous injection of a sedative (e.g. thiopental, propofol, diazepam or midazolam) or narcotic (e.g. morphine, fentanyl, alfentanyl) agent to induce anesthesia; sometimes ketamine is used for this purpose. At the same time, the patient receives a non-depolarizing curare-like drug (e.g. vecuronium or D-turbocurarine) to induce muscle paralysis; sometimes a depolarizing drug like succinylcholine is used for this purpose. Then the patient is intubated and connected to a ventilation machine for artificial respiration. During the surgery, anesthesia is maintained by a mixture of oxygen and nitrous oxide, often combined with a volatile agent such as halothane, enflurane or isoflurane, or an i.v. narcotic. At the conclusion of the procedure, muscle relaxation is reversed by neostigmine or other anticholinesterase agent, and the respirator is removed when unassisted breathing is restored. On the way to the recovery room, the patient may be given an analgesic agent such as morphine for relief of post-operative acute pain. Although the precise combination of drugs varies (depending on the circumstances of the case and the preferences of the physicians), this general technique, known as *balanced anesthesia*, achieves its effect by a combination of sedation, analgesia and muscle relaxation.

The controlled coma known as general anesthesia is typically indicated by: (1) the lack of motor response to instructions; (2) suppression of autonomic and skeletal responses to intraoperative stimuli such as incisions; (3) absence of retrospective awareness of pain; and (4) post-operative amnesia for surgical events such as conversations among the medical team. Nevertheless, there has long been speculation about the degree to which even adequately anesthetized patients retain some ability to process events occurring during the time of their surgery.

This conjecture has been abetted by the simple fact that our knowledge of the mechanisms underlying anesthesia is incomplete. It is possible, at least in principle, that the patient retains full awareness of what is going on, pain and all; but that these experiences are subsequently lost to an anterograde amnesia produced by the anesthetic cocktail; or, more horribly, to a retrograde amnesia associated with post-traumatic stress disorder. The concern with patient awareness is reinforced by occasional episodes of what Bennett (1988) has called the "fat lady syndrome"—cases in which a member of the surgical team has made an unkind remark about the patient on the operating table, after which the patient takes a turn for the worse, develops an inexplicable dislike for the surgeon or the like. Such evidence is all anecdotal, of course, and hard to pin down precisely.

Explicit and implicit cognition

In the past, the possibility of information processing during general anesthesia has been rejected at the outset by many, if not most, anesthesiologists on the grounds that adequately anesthetized patients are unconscious *by definition*. Therefore, such outcomes are impossible—unless the patients were inadequately anesthetized to begin with. However, this response ignores a rapidly building body of laboratory research supporting the concept of information processing outside of awareness (for reviews, see Kihlstrom, 1987, 1990).

For example, presentation of a list of words can be shown to affect the performance of brain-damaged patients with the amnesic syndrome on various sorts of language-processing tasks, even though these patients cannot consciously remember the words themselves. In a typical study, for example, patients study a list of words including PROMOTE and TABOO. Later, after a period of distraction, they are presented with stems such as PRO__ and TAB__, and asked to recall the corresponding words from the study list. Performance on such a test is very poor. Then, they are presented with the same stems, and asked merely to complete them with the first word that comes to mind. Under these circumstances, the patients will be more likely than controls to produce PROMOTE (as opposed to the more familiar PROBLEM) or TABOO (as opposed to TABLE). This is what is known as a *priming effect*, and in the present case priming shows the influence of a past event that the person cannot remember.

Such research supports a distinction between explicit memory, which requires the conscious recollection of a previous episode, and implicit memory, as revealed by a change in experience, thought or action that is attributable to such an event, regardless of whether the event itself is consciously remembered (Schacter, 1987). Note that in the cued recall task, the subject must consciously retrieve information about a specific prior experience. But in the stem-completion test, no such recollection is necessary. Explicit and implicit memory are dissociable, in at least two different senses. First, experimental studies of both organic and functional amnesia show that explicit memory can be grossly impaired while implicit memory remains largely spared. Such effects have been found with neurological patients suffering the amnesic syndrome and various dementing illnesses; they have also been found in post-hypnotic amnesia; but, interestingly, they have not yet been found in sleep. Second, different experimental manipulations affect explicit and implicit memory differently. For example 'deep' processing, involving meaning analyses and other forms of elaborative and organizational activity, favor explicit memory, but have little effect on implicit memory. And a shift in modality of presentation, for example, from auditory presentation to visual test, affects implicit memory, but has little effect on explicit memory. Similarly, events can have an impact on task performance even though these events are not consciously perceived—a phenomenon that we have come to call 'implicit perception' (Kihlstrom, Barnhardt and Tataryn, 1991). For example, words rendered consciously imperceptible by tachistoscopic presentation and/or backward masking may nonetheless facilitate performance on a lexical decision task with the same or semantically related words.

Implicit memory after surgical anesthesia

The significance of these demonstrations is that it can no longer be assumed, on an *a priori* basis, that the overt unresponsiveness of the patient to surgical events, and the patient's inability to remember these events post-operatively, necessarily mean that these events have not been processed to some degree, and thus remain available in memory to influence experience, thought and action. Thus, the question of the degree to which information processing is possible during adequate surgical anesthesia must be considered an open one (for reviews, see Adam, 1979; Bennett, 1988; Kihlstrom and Schacter, 1990; Kihlstrom, Couture and Schacter, 1991; Trustman, Dubovsky and Titley, 1977; for collections of related readings, see Bonke, Fitch and Millar, 1990; Hindmarch, Jones and Moss, 1987; Jones, 1989; Rosen and Lunn, 1987). Although the evidence is still rather mixed, several recent studies employing procedures derived from the laboratory study of implicit memory in neurological patients and normal subjects suggest that a dissociation between explicit and implicit memory may be obtained under certain conditions of adequate anesthesia.

For example, in an early study by Millar and Watkinson (1983), patients maintained on nitrous oxide–oxygen and, in some cases, halothane, were presented a list of low-frequency words during surgery. They showed no post-operative memory for the word list, as measured by a conventional free recall test. However, when given a recognition test and encouraged to guess which items had been presented, these patients showed greater accuracy than control subjects who heard nothing but radio static. The difference is small, but it is statistically reliable. The left-hand panel of Fig. 1 shows that the patients in the experimental group have a significantly higher average d', a signal detection index of accuracy, than the controls. There is a difference in bias, as measured by β, as well; but this indicates that the experimental patients were more conservative than the controls in making recognition judgments. The same trends are documented in the right-hand panel, using non-parametric measures of sensitivity and bias.

While recognition is usually considered to be a measure of explicit memory, research by Mandler (1980) and others suggests that when subjects are encouraged to guess, recognition has a strong 'implicit memory' component. That is, an event may be correctly recognized just by virtue of a vague feeling of familiarity, rather

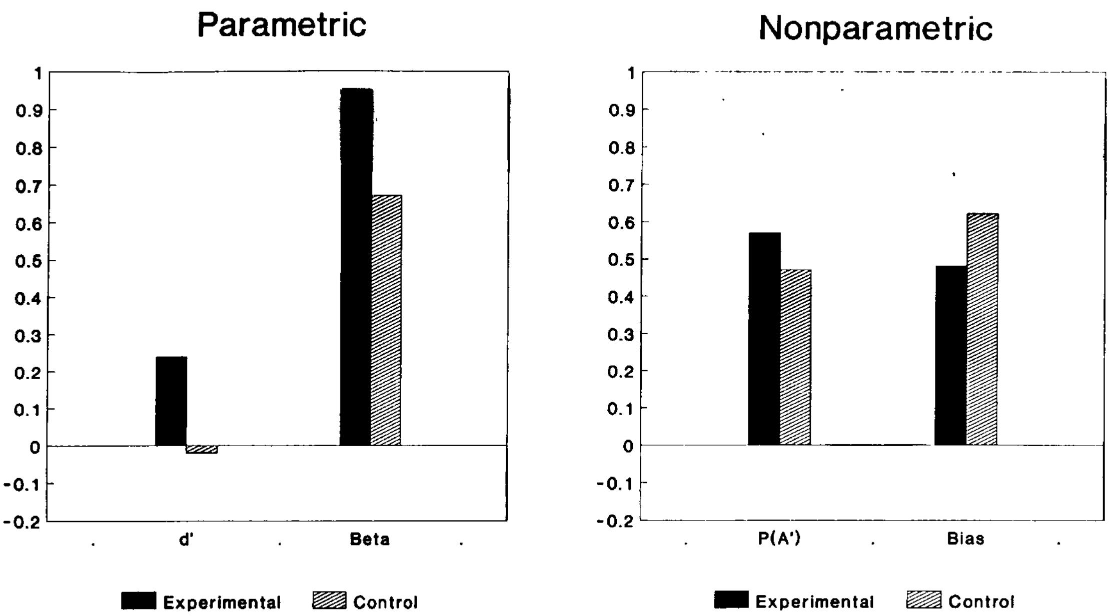

Figure 1 Measures of d' and β in post-operative recognition. Data from Millar and Watkinson (1983)

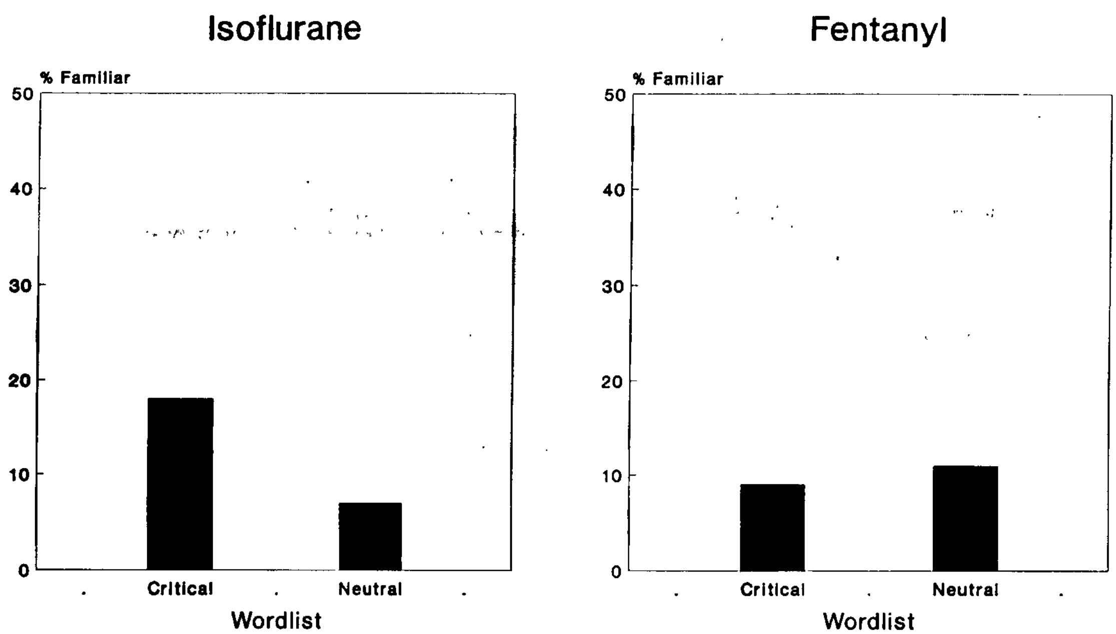

Figure 2 Familiarity ratings for low-frequency words presented during anesthesia with isoflurane and fentanyl. Data from Stolzy, Couture and Edmonds (1986, 1987)

than by a conscious recollection of an event that occurred at a particular time and in a particular place. In other words, performance on the recognition task may have been mediated by a sort of priming effect, rather than true recognition in the usual sense of that term.

This sort of feeling of familiarity is shown nicely in another study, as yet unpublished, conducted by Stolzy, Couture and Edmonds (1986, 1987). Patients anesthetized with isoflurane were presented with a list of extremely low-frequency words (e.g. coruscate and tergiversation), repeated 19 times. Following recovery, a standard recognition test showed that the patients were unable to remember having heard these words during surgery. However, when asked to review the words and circle any that they found 'familiar', they chose words presented during surgery more frequently than carefully matched control words. The left-hand panel of Fig. 2 shows that patients chose ~18% of the words that had been presented during their surgery, compared to only ~7% of control words. This, again, is a priming effect of the intraoperative events on post-surgical task performance. Interestingly, as the right-hand panel of Fig. 2 shows,

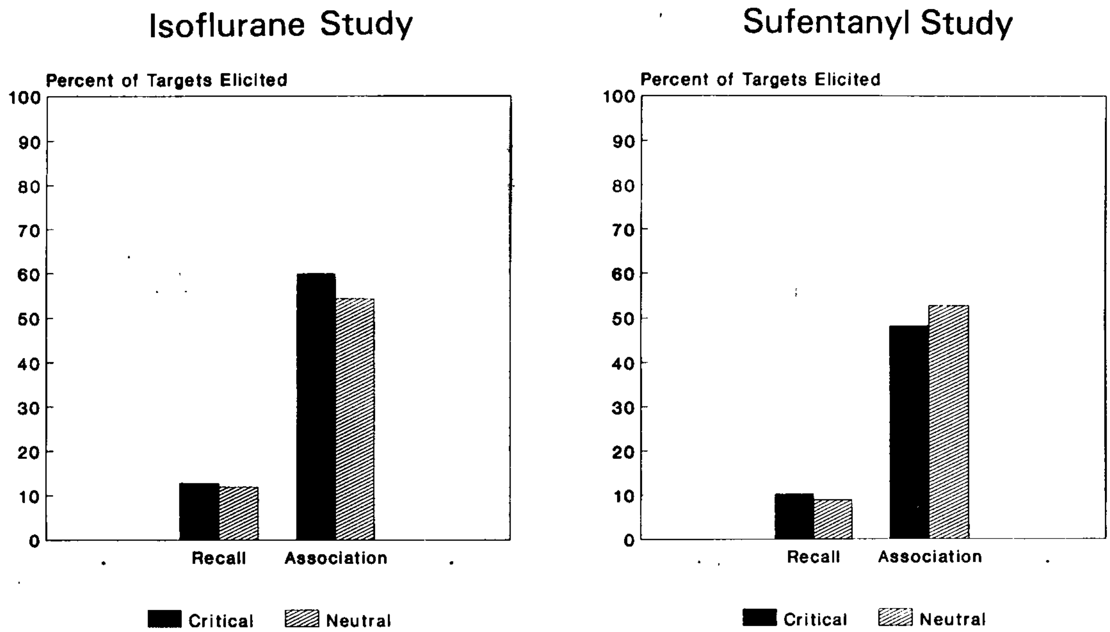

Figure 3 Cued recall and free association performance after anesthesia with isoflurane and sufentanyl. Data from Kihlstrom *et al.* (1990) and Cork, Kihlstrom and Schacter (1992)

this priming effect was not observed in a subsequent replication study, when the anesthetic was switched to fentanyl.

That the anesthetic agent may make a difference to the outcome is also indicated by a pair of studies performed by Kihlstrom, Cork and Schacter. In the first study (Kihlstrom *et al.*, 1990), patients maintained on isoflurane were presented paired associates of the form *ocean–water*. During post-operative testing, the patients were presented with the first word of each pair, and asked to recall the item with which it had been linked. As the left-hand panel of Fig. 3 shows, cued recall was very poor. The results were different, however, when the patients were presented with the cue term, and simply asked to say the first word that came to mind. On this free association test, the patients were more likely to produce items from the list presented during surgery—another priming effect. We should say, in passing, that the overall effect displayed in the left-hand panel is obscured somewhat by an effect of test order. For those who got the implicit test before the explicit test, fully 85% of the patients showed priming. The right-hand panel of Fig. 3 shows the results of a precise replication using sufentanyl (Cork, Kihlstrom and Schacter, 1992): here, there was no evidence of either explicit or implicit memory, even if you take account of the order effect.

We note, however, that some well-designed studies have failed to find the hypothesized dissociation between explicit and implicit memory. One such case is an experiment by Eich, Reeves and Katz (1985). They presented their patients with a list of homophones (e.g. *piece* and *peace*, *sea* and *see*), accompanied by a disambiguating context (e.g. *war* and *peace*; *deep sea*). Under ordinary circumstances, priming effects from such an experience would bias the manner in which the homophones were spelled, regardless of whether the words were consciously remembered. The left-hand panel of Fig. 4 shows the results of conventional recognition testing: while patients who were presented the words pre-operatively showed quite good explicit memory, those who heard the words intraoperatively did not. However, the right-hand panel of Fig. 4 shows exactly the same pattern of performance on the implicit memory test. Pre-operative patients show the expected bias in spelling list items, but intraoperative patients show no priming at all. In this study, then, anesthetized patients showed neither explicit nor implicit memory for the list items.

One important factor determining outcome may be the selection of the anesthetic agent: the positive outcomes reported by Millar and Watkinson (1983), Stolzy *et al.* (1986, 1987) and Kihlstrom *et al.* (1990) were all obtained with inhalant anesthetics. Moreover, Kihlstrom and his colleagues omitted the use of benzodiazepine pre-medication, which may impair both explicit and implicit memory (Ghoneim and Mewaldt, 1990). Practical considerations forced Eich to test a miscellany of patients, some of whom got inhalants while others got narcotics, and most or all of them received pre-operative benzodiazepine. Had Eich been able to confine his sample to patients who received inhalants, and if he had been able to avoid sedative pre-medication, his results might well have been different.

This conclusion must remain tentative, however, because some laboratories have reported dissociations

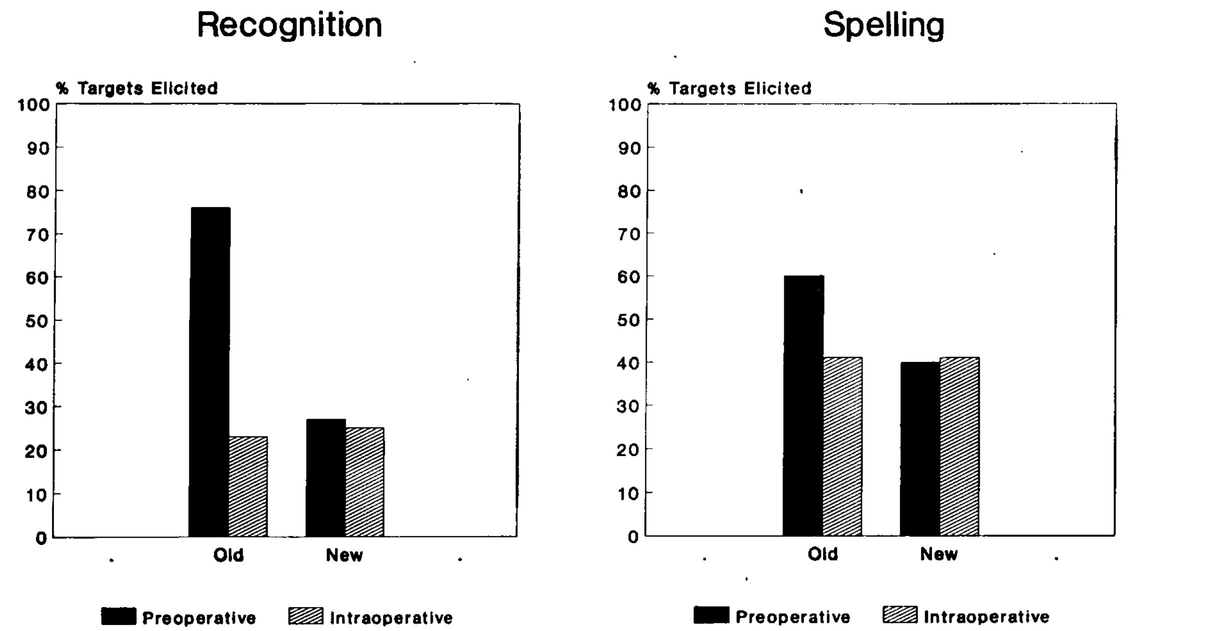

Figure 4 Recognition memory and spelling performance for homophones presented during anesthesia. Data from Eich, Reeves and Katz (1985)

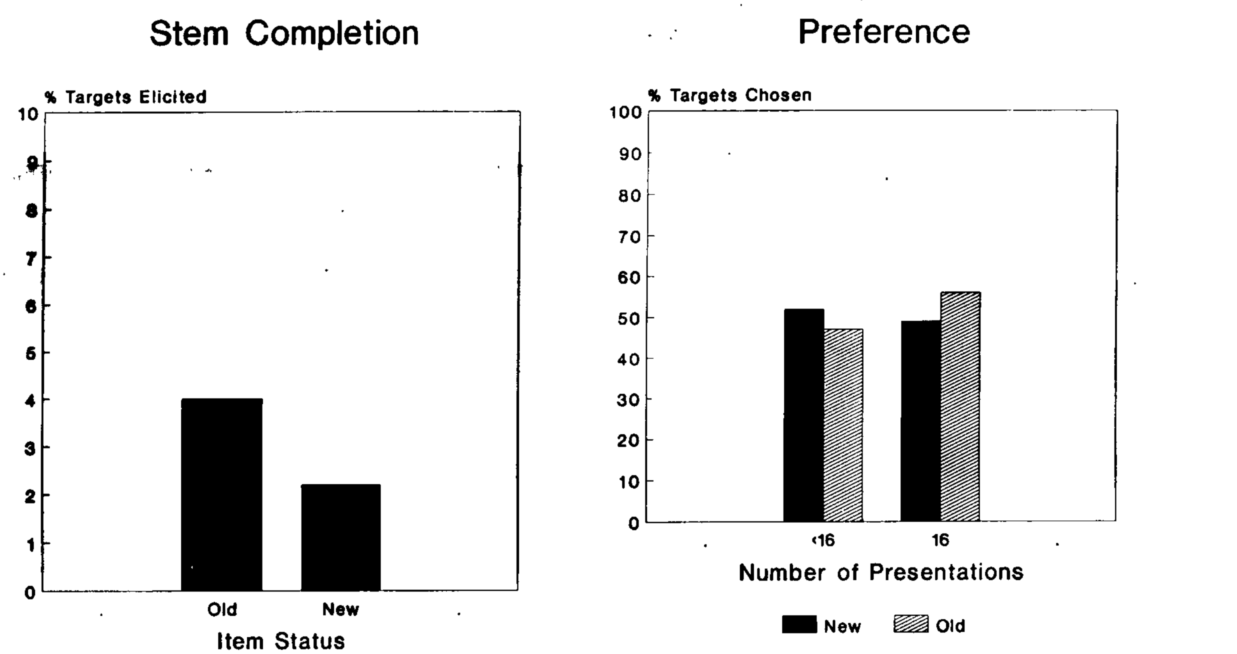

Figure 5 Stem completion and likeability judgments for words presented during anesthesia. Data from Block *et al.* (1991)

between explicit and implicit memory with both inhalant and narcotic regimes (Block *et al.*, 1991; Jelicic, Bonke and Appelboom, 1990; Roorda-Hrdlicova *et al.*, 1990). For example, in the first of two studies reported by Block *et al.* (1991)—the second involved only isoflurane—half the patients received isoflurane, while the others received a nitrous-narcotic preparation. A list of words was played to the patients during their surgery, followed by tests of explicit and implicit memory. In terms of explicit and implicit memory, no patient had any ability to recall or recognize list items. However, the patients showed significant priming on two different tests. The left-hand panel of Fig. 5 shows their performance on a stem completion task involving the meaningful words: they were much more likely to produce a word presented during surgery, compared to a control word. The priming effect on stem completion is of course a classic manifestation of implicit memory, and Block *et al.* report that, while weak, it was obtained in both studies regardless of anesthetic technique.

Block *et al.* (1991) introduce a further complication, in that they used multiple measures of implicit memory, and not all showed priming effects. For example, they also presented their patients with a list of meaningless pseudowords (e.g. BALAP). Later, the patients were shown these words, along with matched items that were entirely new. It has been shown that, when asked to make likeability judgments, subjects tend to prefer items to which they had previously been exposed—regardless of whether they consciously perceived the stimuli at the time, or whether they consciously remembered them later. This *mere exposure effect* (Zajonc, 1968) is another demonstration of implicit memory. Block and Ghoneim report that their anesthetized patients showed a significant mere exposure effect. However, as illustrated in the right-hand panel of Fig. 5, this was so only for those items that had been presented 16 times during surgery; fewer presentations produced no such effect. Moreover, this effect, obtained in the first study, was not confirmed in the second. So now we have to pay attention not only to the particular anesthetic technique employed, but also to the details of the implicit memory test. Apparently, those of us who want to pursue this effect are in for a long and arduous series of parametric studies.

Still, until we know more about this phenomenon, the important point is that the anesthetic agents must be controlled, and their effects studied separately. After all, not all anesthetics are the same. The extremely wide variety of pharmacological compounds routinely employed in anesthetic practice differ not only in terms of molecular structure, but also in their effects on central, autonomic and skeletal nervous system functions. Couture and Edmonds (1989) have attempted a classification of anesthetic agents not on the basis of their chemical composition, but rather on the basis of their physiological and psychological effects. Their analysis indicates that some agents (e.g. the halogenated ethers and barbiturates) produce a generalized depression of most autonomic functions. Others (e.g. fentanyl and other narcotics) produce specific central nervous system effects but exert little or no direct influence on cardiovascular and neuromuscular functioning. A third class (e.g. diazepam and other benzodiazepines) selectively depresses certain CNS, cardiovascular and musculoskeletal functions. The fourth class (e.g. ketamine and etomidate) produces a profound disorganization of CNS functions, as measured by electroencephalographic and other cerebral metabolic indices, and stimulates cardiovascular and neuromuscular activity while having little effect on respiratory mechanisms. The differing physiological effects of these treatments suggest that they may have different psychological effects as well. For example, ketamine often produces hallucinations, but these sequelae are rarely if ever observed with inhalational agents.

Prospects for future research

In any event, the preservation of information processing functions during adequate general anesthesia may have some practical implications. For example, there is now good evidence that at least some patients can respond positively to hypnotic-like therapeutic suggestions administered during anesthesia, showing speeded post-operative recovery, diminished requests for pain medication and the like, although the patients do not remember receiving the suggestion. Pearson (1961) demonstrated this effect >30 years ago, and more recent double-blind studies by Evans and Richardson (1988) and by Furlong (1990), have confirmed his observations under more tightly controlled conditions. Because these psychosomatic effects result from suggestions delivered during anesthesia, they also count as information processing and constitute a bodily expression of implicit memory. Unfortunately, these positive findings are not completely reliable, suggesting that the conditions under which such suggestions work remain unknown (McClintock *et al.*, 1990; Woo, Seltzer and Marr, 1987; Boeke *et al.*, 1988). Moreover, as in the case of hypnosis (Bowers, 1977; Bowers and Kelly, 1979; Johnson, 1990), the mechanism by which such suggestions work remains a mystery.

The limits of these implict memory and psychosomatic effects, and the precise conditions under which they may be obtained, remain a topic for future research. For example, some tests used by Block and Ghoneim showed evidence of implicit memory, but others did not, suggesting that there are unknown task factors. Furthermore, it is not yet known to what extent post-anesthetic implicit memory is limited to the activation of old knowledge, or can extend to the encoding of novel information. The preference-rating task employed by Block *et al.* (1991), and a similar task involving music (Winograd *et al.*, 1991), involves the acquisition of new knowledge, and does not provide evidence of implicit memory; however, the studies by Millar and Watkinson (1983) and Stolzy, Couture and Edmonds (1986) employed extremely low-frequency words, which may have been entirely new to at least some of the subjects. Recent research by Bonke and his colleagues has begun to address this issue directly; but more needs to be done.

However, even if future research continues to provide convincing evidence for implicit post-operative memory (including the effects of intraoperative therapeutic suggestions), it is important to recognize that such a situation would not necessarily undermine the concept of adequate anesthesia. There is a difference between cognition and consciousness, and a great deal of evidence supports the notion that some degree of information processing can proceed outside of phenomenal awareness. Outside of the very provocative results obtained by Russell (1990) and others with the isolated forearm technique, there is little reason to think that adequately anesthetized patients are aware of what is happening to them at the time it is happening.

However, it is fairly clear now that at least some forms of general anesthesia are not properly described as a total lack of consciousness, as previously assumed. Rather, they may be better described as states of *altered* consciousness, entailing a dissociation between explicit and implicit memory. Thus, anesthetized patients lack concurrent or retrospective awareness of surgical events; yet these events may be processed, at least to some degree, and their residual traces may affect the patient's subsequent experience, thought and action. Moreover, it appears likely that different anesthetic agents may produce different altered states, with different patterns of effects on implicit memory. We expect that continued study of drug effects on explicit and implicit memory, coupled with a better understanding of the anatomical sites and physiological mechanisms of various anesthetic drugs, will complement standard neuropsychological and brain-imaging studies, and bring us closer to a psychobiology of cognition and consciousness.

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