Anesthesia: Effects on Cognitive Functions

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Surgical anesthesia is intended to render the patient insensitive to pain. In a typical clinical procedure ("balanced anesthesia," involving sedation, analgesia, and muscle relaxation), the patient may be premedicated with a sedative (chiefly benzodiazepines such as diazepam), to relieve preoperative anxiety and facilitate the induction of anesthesia. This is followed by the intravenous injection of a sedative (e.g., thiopental, propofol, diazepam, midazolam) or narcotic (e.g., morphine, fentanyl, alfentanyl) drug, or ketamine as well as a nondepolarizing curare-like derivative (e.g., vecuronium, d-turbocurarine) or a depolarizing drug (e.g., succinylcholine) to induce muscle paralysis. After intubation and connection to a ventilator for artificial respiration, anesthesia frequently is maintained by a mixture of oxygen and nitrous oxide, often in combination with a volatile agent (e.g., halothane, enflurane, or isoflurane) or intravenous drugs. At the conclusion of the surgery, muscle relaxation is reversed (e.g., by neostigmine or other anticholinesterase), and normal (unassisted) breathing is restored. In addition, the patient may be given an analgesic agent (e.g., morphine) to manage any acute pain experienced postoperatively.

A wide variety of pharmacological compounds are routinely employed in clinical practice: these differ in molecular structure as well as in their effects on central, autonomic, and skeletal nervous system functions. Some agents (e.g., halogenated ethers, barbiturates) produce a generalized depression of most autonomic functions. Others (e.g., fentanyl) produce specific central nervous

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system (CNS) effects but exert little or no direct influence on cardiovascular and neuromuscular functioning. A third class (e.g., benzodiazepines) selectively depresses certain CNS, cardiovascular, and musculoskeletal functions, and a fourth (e.g., the ketamines, 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. One implication of these findings is that physiological responsiveness, as an index of anesthetic adequacy, is multidimensional, and monitoring of any single system may be insufficient.

General anesthesia operates directly on the central nervous system, producing (at least in theory) a temporary inhibition on synaptic transmission that results in general loss of consciousness that affects sensory awareness in all modalities and at all body loci. This "controlled coma" is indicated by: a) the lack of motor response to instructions, b) suppression of autonomic and skeletal responses to intraoperative stimuli such as incisions, c) absence of retrospective awareness of pain, and d) postoperative amnesia for surgical events such as conversations among the medical team. Thus, by definition, adequately anesthetized patients rarely show any conscious recall or recognition of surgical events. Nevertheless, there is some evidence that surgical events may be processed to some degree even by adequately anesthetized patients, resulting in the encoding of memory traces of experience that can affect subsequent task performance.

Prima facie evidence for information processing during general anesthesia is provided by studies of classical conditioning in animals: conditioned fear responses can be acquired during anesthesia and displayed after recovery. This evidence is mitigated, however, by the empirical fact that conditioned responses can be established in almost any organism that has a nervous system, including decorticate animals. This primitive form of learning should not be confused with the higher cognitive processes involved in intelligent perception, memory, and thought.

Other evidence indicates that adequately anesthetized patients continue to show event-related potentials (ERPs) to auditory and tactile stimulation. In fact, intact ERPs constitute one way in which the patient's status is monitored during surgery. However, the ERP is very complex: for example, the first 10 msec of the auditory ERP reflect brain stem activity, those arising within 10 to 100 msec reflect the activity of the primary auditory cortex, and those observed after 100 msec reflect the activity of the cortical association areas. Only the early components of the ERP are unaffected by anesthetic agents (and these are the only components routinely monitored during surgery); the later, perceptual–cognitive components exhibit dose-related suppression of activity. To date there have been no studies of the fate of later components of the cognitive ERP, such as the P300 response to the omission of an expected event or the N400 response to semantic anomalies.

Without studies of cognitive ERPs, on-line evidence of complex mental activity comes primarily from studies using the "isolated forearm technique," in which muscle relaxant is prevented from affecting one arm by means of a tourniquet. In some (but not all) cases, the patient retains the ability to make a motor response with the spared limb in accordance with instructions from the anesthetist. Moreover, patients can respond to instructions given during anesthesia after recovering consciousness. In either case, such responses provide evidence that the instructions themselves were heard during surgery. However, adequately anesthetized patients have no conscious recollection of having been given these instructions.

Evidence of information processing *during* anesthesia may be provided by evidence of memory *afterward.* Of course, a failure to remember surgical events is part and parcel of the definition of adequate anesthesia. However, recent studies of both brain-damaged patients and intact individuals support a distinction between explicit memory, which requires the conscious recollection of a previous episode, and implicit memory, as revealed by a change in task performance that is attributable to such an event, regardless of whether the event itself is consciously remembered. By definition, adequate general anesthesia abolishes explicit memory for surgical events, but the possibility remains that some degree of implicit memory may be spared.

Although the evidence is still rather mixed, recent studies employing procedures derived from the laboratory study of normal and pathological memory suggest that a dissociation between explicit and implicit memory may be obtained under certain conditions of adequate anesthesia. For example, patients (maintained on nitrous oxide oxygen and, in some cases, halothane) who were presented a list of low-frequency words during surgery showed no memory for the list on a postoperative recall test, but when encouraged to guess on a recognition test, showed greater accuracy than controls. In another study, anesthetized patients (isoflurane) who were presented with a list of extremely low-frequency words were unable to remember these words after recovery but they did rate these items as more familiar than carefully matched control words (this effect was not observed when the anesthetic was switched to fentanyl). Finally, patients (maintained on isoflurane) who were presented paired associates showed no subsequent free recall, cued recall, or recognition of the items, but they were more likely to produce list items on a free-association task, compared to controls. We note, however, that several well-designed studies have failed to find such effects. One important factor determining outcome may be the selection of the anesthetic agent: the positive outcomes described have all been obtained with inhalant anesthetics. Another may be the use of benzodiazepine premedication, which is known to impair both explicit and implicit memory.

The preservation of information-processing functions during adequate general anesthesia has some potential practical implications. For example, there is good evidence that at least some patients respond positively to therapeutic suggestions administered during anesthesia, showing speeded postoperative recovery, diminished requests for pain medication, and the like, although the patients do not remember receiving the suggestion. These psychosomatic effects also count as evidence of information processing during anesthesia, as well as of implicit memory. Unfortunately, as in hypnosis, the mechanism by which such effects are achieved is unknown.

In closing, we must note that "general anesthesia" is not a single, monolithic construct. It seems likely that the various types of anesthetics in current use have different psychological effects as well. Thus, isoflurance appears to spare implicit memory to some degree, whereas diazepam and fentanyl in combination appear to affect both explicit and implicit memory. Detailed study of the cognitive effects of the various classes of anesthetic agents, coupled with a more detailed psychopharmacological theory of anesthetic effects, may yield important insights into the biological substrates of conscious and nonconscious cognitive processes.

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Further reading

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