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, known as balanced anesthesia, the patient is premedicated with a sedative intended to relieve preoperative anxiety and facilitate the induction of anesthesia itself. Often this premedication is a benzodiazepine such as diazepam or midazolam; otherwise, a barbiturate such as thiopental or a nonbenzodiazepine such as propofol may perform this function. Sedation is followed by the induction of general anesthesia by intravenous injection of a sedative, narcotic (e.g., morphine, fentanyl, or alfentanyl), or ketamine. In addition, a nondepolarizing curare-like derivative (e.g., vecuronium or d-tubocurarine or a depolarizing drug (e.g., succinylcholine) is administered to induce muscle paralysis. After intubation and connection to a ventilator for artificial respiration, general anesthesia may be maintained by a mixture of oxygen and nitrous oxide, often in combination with a volatile agent (e.g., halothane, enflurane, or isoflurane) or an intravenous narcotic. 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.

In contrast to local anesthesia, which affects the peripheral sensory nerves in particular bodily locations, general anesthesia operates directly on the central nervous system, producing a general loss of consciousness that affects sensory awareness in all modalities and at all body loci. This "controlled coma" is indicated clinically 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) 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 surgery. In fact, the incidence of intraoperative awareness in general surgical cases has been estimated at approximately 0.15% for general surgical cases (Sandin, Enlund et al. 2000), increasing somewhat in cardiac surgery, obstetrics, and especially trauma surgery, where lower doses of anesthetics are used. 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 postsurgical experience, thought, and action.

1. On-line evidence

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. However, 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 somatosensory stimulation. In fact, intact ERPs constitute one way in which the patient's status is monitored during surgery, supplementing autonomic signs such as blood pressure, heart rate, sweating, and tears (Sigl and Chamoun 1994; Thornton and Sharp 1998). However, the ERP is very complex (Hillyard and Kutas 1983). Only the early, subcortical components are clearly unaffected by anesthetic agents (these are the only components routinely monitored during surgery); the later, perceptual and cognitive components exhibit dose-related suppression of activity. To date, there have been few studies of the fate of the cognitive ERP, and the few studies relating intra-operative ERPs to postoperative memory have yielded ambiguous results (Schwender, Klasing, et al. 1993).

In the absence of definitive 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 (Jessop and Jones 1991). In a substantial minority of cases, the patient retains the ability to make a motor response with the spared limb in accordance with instructions from the anesthetist. However, the vast majority of adequately anesthetized patients have no conscious recollection of having been given these instructions. While the isolated forearm technique provides evidence of some degree of intraoperative awareness, it should be noted that most studies with the technique are in obstetrical procedures where relatively light doses of anesthesia are used.

2. Retrospective evidence

Evidence of information processing *during* anesthesia is often sought in 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 subjects 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 (Schacter 1987). While amnesic patients typically fail to recall or recognize the items studied in a list of words; they generally show priming effects attributable to the study episode when they are asked to identify words presented under degraded conditions, or words as completions of stems or fragments. 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, some 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 (Ghoneim and Block 1992; Andrade 1995; Ghoneim and Block 1997). In one study, adequately anesthetized patients maintained on isoflurane who were presented paired associates of the form *bread-butter* over earphones during surgery showed no subsequent free recall, cued recall, or recognition of the items during postoperative testing (Kihlstrom 1990, Schacter, et al. 1990). However, when presented with the first term of the pair and asked to report the first word that came to mind, they were more likely to produce the second term than were controls. However, a subsequent study by the same team, employing the same methods with patients maintained on sufentanil and nitrous oxide, yielded negative results (Cork, Kihlstrom, et al. 1992).

As the discrepancy between these two studies suggests, implicit memory for events occurring during general anesthesia remains controversial. The situation is complicated by wide variation from laboratory to laboratory in type of surgery, anesthetic cocktail, techniques for monitoring anesthetic depth, and tests of implicit memory. However, a 1996 meta-analysis of 44 studies clearly showed that repetition priming is relatively spared under adequate anesthesia (Merikle and Daneman 1996). However, there is little evidence for spared semantic priming. This conclusion is consistent with the idea that variations in depth of anesthesia may permit some "automatic" perceptual processing of surgical events, but not complex meaning analyses. Along these lines, there is some evidence that implicit memory is increased when physiological stress responses to surgical stimuli such as incisions adventitiously improve the circumstances of memory encoding (Stapleton and Andrade 2000). Implicit memory also appears to be greater with inhaled anesthetics, or lighter planes of anesthesia. The relation of postoperative implicit memory to intraoperative ERPs is ambiguous at present (Schwender, Klasing, et al. 1993).

In *conscious sedation*, a technique that is increasingly popular in outpatient surgery, the patient receives sedatives and analgesics but not inhalant or narcotic anesthetics. As a result, the patient remains awake throughout the procedure, and can interact with the surgical team. However, the sedatives employed frequently render patients amnesic for their experiences, a condition something like alcoholic blackout. However, as in general anesthesia, this amnesia affects explicit memory, but not implicit memory (Polster 1993). For example, one study showed significant priming on a free-association task in patients who were sedated with propofol, a synthetic drug with sedative effects similar to those of benzodiazepine (Cork, Heaton, et al. 1996).

3. Therapeutic suggestions

Early findings that adequately anesthetized patients could make postoperative motor responses to cues arranged during surgery (Bennett, Davis, et al. 1985) have not been confirmed by subsequent research (Dwyer, Bennett, et al. 1992). Nevertheless, the possibility of spared implicit memory has suggested that patients might respond to therapeutic suggestions administered during anesthesia with improved postoperative course. Again, occasional positive results, showing speeded postoperative recovery, diminished requests for pain medication, and the like (Bonke, Schmitz et al. 1986; Evans and Richardson 1988), were not confirmed in the 1996 meta-analysis (Merikle and Daneman 1996). Although the sparing of implicit memory warrants further study of this issue, the likelihood that patients can respond positively to specific suggestions administered during adequate anesthesia is diminished by the absence of semantic priming in implicit memory. Adequate anesthesia almost certainly precludes the sort of semantic analysis that would be required for such an outcome.

Some patients, and their physicians, are disturbed by *any* evidence of postoperative memory for surgical events (Schwender, Kunze-Kronawitter, et al. 1998). However, evidence of postsurgical implicit memory does not imply that ostensibly anesthetized patients are in fact aware of surgical events as they occur. Rather, they indicate only that some degree of perceptual processing can proceed outside of awareness, even under conditions of adequate anesthesia. Implicit memory following adequate anesthesia is revealed under only very special conditions. Although accidental surgical awareness leading to explicit memory for surgical events and posttraumatic stress disorder is not a trivial problem, and can have significant medicolegal consequences (Domino, Posner, et al. 1999), evidence that surgical events can unconsciously influence patients' real-world experiences, thoughts, and actions (Levinson 1965) remains at the anecdotal level (Chortkoff, Gonsowk, et al. 1995).

Although the preservation of implicit memory in general anesthesia and conscious sedation may not have much practical significance, research on anesthetic agents may play an important role in cognitive neuroscience, especially with respect to uncovering the neural correlates of consciousness. For example, at the molecular and cellular level of analysis, anesthesia has been viewed as the result of generalized inhibition of synaptic transmission, perhaps through effects on protein receptors for certain neurotransmitters, or on the production of neurotransmitters themselves (Hameroff and Penrose 1996). At the systems level, it has been proposed that anesthetics act through portions of the reticular formation, to inhibit communication from the thalamus to cerebral cortex (John, Prichep, et al. 2001). Although these theories are interesting, it seems likely that different anesthetic agents, such as inhalants and narcotics, have different pharmacological mechanisms of action, with different psychological effects as well. 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.

4. Author notes

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5. See also

Anesthesia, mechanisms of

Anesthesia, nerve block

Cognition, unconscious processes

Learning and memory

Author's website:
http://www.socrates.berkeley.edu/~kihlstrm

6. Further reading

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Information on the 5th conference, held in New York in 2001, and the 6th conference, scheduled for Hull, U.K., in 2004, is available on the Internet at http://www.maacc.org.

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