Medical Intelligence

Anesthesia and Memory Processes

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Amnesia for the events occurring during surgical
operations is a desirable feature of general an-
esthesia but is not always attained. Evidence
from research on memory suggests that anesthetic
amnesia results from 1) attenuation of sensory
transmission and 2) impairment of the ensuing
memory-consolidation process. In a few patients,
however, auditory information of high emotional
content, coinciding with a lightening of anes-the-
sia, results in memory consolidation sufficient to
permit unpleasant recall, spontaneously or under
hypnosis. The physiologically desirable light lev-
els of modern anesthesia impose the constraint of
avoiding conversation in surgery that can result in
psychologically undesirable memory traces. (Key
words: Amnesia; Anesthesia; Memory.)

It is well known that anesthetic agents affect
memory; the amnesic effect of nitrous oxide
was reported by Humphry Davy in 1799, and
anesthetic amnesia was noted by John Snow in
1847. Today’s anesthesiologist seeks to protect
patients from unpleasant memories of sur-
geal operations, but this goal is not always at-
tained.1-28 Whether every patient needs such
protection is a matter of opinion. Many pa-
tients undergoing spinal or regional block an-
esthesia can remember the happenings in the
operating room with equanimity. On the other
hand, even memories that can be recalled only
under hypnosis 17-22 have been claimed to be
psychologically traumatizing and physiologically
damaging.6-8 Reports of troublesome memory retention 1, 2, 12, 13, 19, 25, 28 began to increase after d-tubocurarine was in-
roduced in 1942, and recent interest has been
widespread.4, 10, 14, 21, 23-27

That postoperative recall of events during
the operation can be prevented by light anes-
thesia is well documented.24, 26-32 However,
the fact that recall is not always prevented by
seemingly adequate anesthesia is also well
documented.1-28 Further, learning in anesthe-
tized animals has been reported 31, 32; such
learning shows that memories can form de-
spite anesthesia.

Two questions need resolution. First, what
mechanism permits an anesthetized patient,
unresponsive to conversation, to form a mem-
ory of that conversation? Second, why does a
patient at a light plane of anesthesia, where
he is responsive to conversation, completely
forget that conversation? This review ex-
amines these apparently contradictory ques-
tions and describes recent research that may
contribute to understanding them. Specifi-
cally, we analyze the roles of attenuated sen-
sory transmission, impaired memory consolid-
ation, and state-dependence, and specify the
combined events that can result in unpleasant
recall, namely, a light level of anesthesia coin-
ciding with acute pain or with auditory infor-
mation of high emotional content.

Sensory Modality

When memory retention after operation does
occur, pain and sounds are recalled most often,
even though pain seems to be the first mo-
dality to be lost in anesthesia.30 The incidence
of memory of pain is highest in patients un-
dergoing procedures known to be acutely pain-
ful.1, 3, 10, 14, 18, 25, 27 Severe pain stimuli may
elicit reflex responses in anesthetized patients
who are unresponsive to ordinarily painful
stimuli; may not the transitory stimulus-pro-
duced lightening of anesthesia progress to the
point where pain is not only perceived but re-
Amnesia occurs when the above train is sufficiently impaired at any point from information input to long-term output. Where do clinical anesthetics exert their amnesic effect?

The simplified “two-store” theory of memory postulates that short-term memory is retained in an unstable form, whereas long-term memory is retained in a consolidated “engram”—a stable, physical, memory trace in the brain. The engram follows a more gradual pattern of growth and decay than the short-term trace. The growth and decay curves may depend to a great extent on the initial strength of the information input. According to the “mnemon” concept, memory is quantal; a “weak” engram has only a few mnemonons (units of memory), whereas a “strong” engram has many mnemonons. The mnemon concept further postulates that recall is not an all-or-none phenomenon; rather, there is a threshold for recall. Weak engrams have subthreshold numbers of mnemonons and cannot be recalled unless the threshold is lowered, e.g., by hypnosis or administration of a “truth serum” (thiopental or scopolamine). Thus, engram formation is a necessary but not a sufficient condition for long-term recall; successful recall requires also that the engram be above threshold. We suggest that the effect of increasing the depth of anesthesia is to decrease the number of mnemonons formed by a given information input and thus to decrease the probability of the engram’s being above threshold.

Information Input, Short-Term Storage and Recall

General anesthesia does not imply a complete block of neural function. The auditory system of the cat and the visual system of the monkey remain functional at planes that depress the reticular formation to the level of unconsciousness. Human subjects recall non-emotional auditory information given during EEG slow-wave sleep. If such findings can be extrapolated to anesthetic sleep, they suggest that input occurs while the brain is in a
state corresponding to EEG slow-wave sleep. Results of several experiments in man give evidence that information input is at least partially resistant to light anesthesia; subjects are responsive to all sensory modalities even though they forget the sensations after the anesthetic wears off. The impairment presumably occurs between short-term and long-term storage.

Anesthesia raises sensory thresholds and reduces the late components of sensory evoked potentials. Thus, the net input from a given external stimulus to the memory-processing system is presumably attenuated by anesthetics, resulting in the formation of a weak engram which rapidly decays to below the threshold level required for recall. The report that patients anesthetized with ether to stage I, plane 2, were conscious and cooperative but were afterwards amnesic for the residual pain is consistent with this interpretation. It is known that weak information input is forgotten sooner than strong input. In the unanesthetized chick, for example, avoidance training with a weak stimulus was forgotten within two days, whereas training with a strong stimulus was remembered for at least nine days.

**Memory Consolidation, Long-term Storage and Recall**

Memory consolidation becomes invulnerable to weak amnesic treatments (anesthesia; weak ECS) about a minute after information input. An hour later, only near-lethal treatments (deep anesthesia; strong ECS; high doses of chemoconvulsants) disrupt consolidation. Anesthetic amnesia is probably not due to depressed transmission alone, however, because during ether or barbiturite anesthesia in animals, painful stimuli still evoke electrical responses in the cerebral cortex (although not in the reticular system), indicating functional transmission. Therefore, impaired consolidation presumably contributed to subsequent loss of recall. A plausible interpretation of incomplete amnesia, then, is that while light anesthesia attenuates sensory transmission and impairs memory consolidation during its vulnerable early stage, the combined effect may not always suffice for amnesia.

**Dose Dependence**

The effect of an anesthetic upon a wide variety of biological functions depends so markedly upon its concentration that its effect upon memory should also be highly dose-dependent. This quantitative aspect is particularly important because 1) low concentrations of anesthetics may stimulate rather than depress and 2) stimulants such as strychnine and picrotoxin can enhance memory retention, suggesting that "stimulant" concentrations of anesthetics might enhance memory. Such an effect has been reported with ether in mice and pentobarbital in rats. Subanesthetic concentrations in man, however, appear to depress memory formation.

Parbrook analyzed the concentration dependence of the amnesic effects of nitrous oxide. Other observations with human volunteers have indicated that nitrous oxide at 0.33 P (i.e., at a third its anesthetizing partial pressure) impaired input or short-term storage, or both, but a more quantitative study using a range of partial pressures (0.2–0.5 P) found no apparent impairment of input or "short-term recall" (30 sec after input). Later recall (2–5 min) was impaired as the partial pressure was raised. Using a similar range of partial pressures of nitrous oxide, Parkhouse et al. found no effect at 0.2 P, equal reductions of short-term and long-term recall at 0.3 P, but only a slightly greater effect on short-term recall at 0.4 P, where long-term recall was abolished. Thus, although evidence for the concentration dependence of nitrous oxide exists, these studies do not permit a clear allocation of its amnesic effects to the impairment of information input, short-term storage, or the early vulnerable phase of consolidation. They underscore the need for clinical studies using careful control of the partial pressures of single anesthetic agents, with and without premedication, with controlled information input and quantitative measures of short-term and long-term recall.

Since the probability of incomplete amnesia after surgical operation is low, perhaps about 1 per cent, individual patient variation must play a major role, and conflicting results are to be expected. Rosen, for example, reports that one patient was fully anesthetized
at 0.4 Pa, whereas another patient at 0.7 Pa remained conscious and had complete recollection of a hearing test.

Premedication
Premedication effects interact with anesthetic effects upon memory. The incidence of unpleasant recall in obstetric patients dropped from 21.1 to 3.1 per cent in patients given narcotic medication within six hours preoperatively; when a tranquilizer (diazepam) replaced the narcotic, the incidence of unpleasant recall rose to 35.5 per cent. Diazepam (Valium) alone (0.24 mg/kg, administered intravenously) impaired recall for at least 30 minutes in volunteers. Crawford et al. recommended replacement of atropine by scopolamine to improve anesthetic amnesia. In contrast, Gruber and Reed studied pre- and postoperative amnesia associated with general anesthesia (thiopental, halothane, nitrous oxide) as a function of preoperative medication (atropine, meperidine, pentobarbital) and concluded that postoperative amnesia was primarily related to the general anesthetic. This point wants more study under controlled conditions.

State Dependence
Overton suggested that "state dependence" might explain the observation that forgotten events which occurred during anesthesia could be recalled under hypnosis. In state-dependent learning, animals trained under the influence of a drug show recall only under the influence of a second dose of the same drug or of certain other drugs. Although Overton originally suggested that similar neural mechanisms might underlie both phenomena, an attempt to demonstrate state dependence with thiopental or hypnosis in man gave negative results and led Overton to reverse his view. Nevertheless, state-dependent recall in man has been detected using amobarbital and alcohol; a study of such recall using inhalation anesthetics is clearly needed.

Conclusion
The evidence for the formation of memory traces during surgical anesthesia is still controversial. Nevertheless, there is a theoretical rationale for the evidence that such formation occasionally occurs under certain circumstances. "Surgical anesthesia" is not a unique state with a single immutable effect upon memory processes. On the contrary, anesthetic amnesia is a probabilistic phenomenon. The major factors that contribute to a high probability of amnesia are uninterrupted maintenance of anesthesia and absence of auditory input of high emotional content. When transient lightening of the anesthetic level coincides with conversation frightening to a patient, the probability of memory consolidation and later recall is increased. Even when voluntary recall does not occur, a memory trace sufficient to permit recall under hypnosis may form. Such a view is consistent with the experimental finding, in animals and in man, that the quantitative extent of retrograde amnesia depends upon both the effective learning strength and the intensity of the amnesic treatment. The wealth of clinical material available to the anesthesiologist suggests that significant contributions to the nature of memory processes may be expected from well-controlled studies of the amnesia of anesthesia.

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References

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Supplementary References—Recent Books on Memory