Memory Function during Anesthesia

WHAT happens to the thinking brain during "general anesthesia"? More specifically, are the higher processes of cognition turned off? Two articles in this issue of anesthesiology show that some form of memory can be formed during what every clinician would call adequate anesthesia.1,2 These findings are in line with many previous investigations in this area. Anesthesia represents a iatrogenic state in which drug-induced "sleep" and memory interact, usually in the setting of the liberal use of muscle relaxants. During clinically adequate anesthesia, the brain is capable of receiving auditory stimuli and of processing them at a fairly complex level, at least in certain cases.3-7 Therefore, the brain, although anesthetized, is functional in the higher cognitive sense. Because we still do not know why the brain sleeps, how anesthesia works, or even the workings of memory, it is no surprise that we cannot figure out what happens to memory and cognition during anesthesia. As with sleep,
anesthesia represents an active brain state yet to be fully defined.

Memory has distinct, separate components with accepted guidelines used to differentiate one type of memory from another. Of interest here are two different forms of memory. Explicit or episodic memories represent the dramatic, increasingly publicized awareness situation in which the patient has a clear recollection of frequently unpleasant experiences. Of more interest, possibly because we do not understand them as well, are implicit memories. The existence of implicit memory as a separate memory system has been postulated for many years. Recent functional neuroimaging techniques are beginning to reveal the anatomic substrates of this form of memory, lending more credence to the separate existence of implicit memory. These memories are not accessible to the conscious mind, but are evident in the subsequent influence of behavior. Unconscious memory function during general anesthesia is frequently labeled as implicit memory. This results from the finding that these memories are not explicitly recalled, and many of the testing procedures used are also those that show implicit memories in nonanesthetized subjects.

Neither study in this issue of Anesthesiology found definite evidence of explicit memory, even in the emergency trauma patients studied by Lubke et al. in which some explicit memory might be expected. To prove that a memory formed during anesthesia is not an explicit one is exceedingly difficult. This problem is admirably and ingeniously tackled by Lubke et al. in part by using a previously described cognitive technique. One of the tenets used in proving that two memory systems are separate is to demonstrate on a test that one form of memory behaves differently, usually in the opposite direction, than another form of memory. The process-dissociation procedure (PDP) does exactly this to isolate implicit memory from explicit memory. The hypothesis is that explicit memory is under conscious control, whereas implicit memory is not. Think of subliminal advertising, a particularly nefarious form of implicit memory. If during a word stem completion test (Cor ____) we are asked to complete a word fragment with the first word that comes to mind (Corvair), this could be either an explicit or implicit memory. If we are asked to complete a word fragment with a different word than the first word that comes to mind, then we obtain some information on implicit memory. If we complete the word stem in this situation with a word that we have been previously exposed to, then implicit memory is present, because by definition we do not know we are recalling it. Using this technique, Lubke et al. have demonstrated that memories formed during anesthesia are implicit in a fashion more convincing than many previous studies.

A nice refinement is the use of Bispectral Index as a concurrent measure of momentary brain state during stimulus presentation. Because memory is likely to involve higher-level cortical processing, it stands to reason that the BIS, measuring cortical electrical activity, should relate in some fashion to the level of function of memory, at least with certain anesthetics. This appears to be the case in the investigation by Lubke et al., because the chance of implicit memory formation was greater at higher levels of BIS. To further indicate the dose-dependence of memory formation on anesthetic state, Lubke et al. applied two fairly complex models of memory to their data. The model that assumes memory varies with a hypothetical depth of hypnosis best explains the memory results obtained. Note that these are models of memory and do not require the actual measurement of the depth of hypnosis to be applied.

As a demonstration of how difficult memory research during anesthesia can be, the article by Munte et al. reports the results of two back-to-back studies. The first used a test, word-stem completion, which has indicated the presence of memory during anesthesia in many previous studies, including the study of Lubke et al. in this issue. The test used by Munte et al. seems to be quite robust, because the expected results were obtained in an appropriate control group. But, no doubt to the chagrin of the investigators, no memory effect was observed in the anesthetized group. How are these results explained? It could be that the anesthetic level was too deep for any memory to occur. This would fit in with the results of Lubke et al. However, we have no information as to the depth of anesthesia at the time of stimuli presentation in the Munte et al. study. Although anesthetic depth was not quantified, Munte et al. have given us the next best thing to actual blood concentrations, which is a pharmacokinetic simulation of their infusion regimens with predicted concentrations, information that will be quite valuable to future investigators.

Another explanation for the lack of memory effects during anesthesia in this study is the minor variations from techniques used by other investigators. These include considerations such as testing recall in a different modality than presentation, the patients becoming aware of the nature of implicit memory testing procedure, using uncommon versus common words, using stems that have unclear pronunciation of the first syll-
ble, among others. An argument against this point is that Munte et al.\(^2\) had the appropriate positive results in control subjects. Munte et al. went on in the next study to use reading speed as a measure of implicit memory, this time more successfully. The differences in reading speed were quite small, but they were statistically significant. It is interesting that this should happen, because the cognitive processes tested in the reading speed test are presumably more complex than those associated with word-stem completion. Does this mean reading speed is a better measure of memory effect during anesthesia than stem completion? One cannot say because these two tests were not studied concurrently in a randomized design in which anesthetic state was quantitated during stimulati presentation.

Perhaps it is time that a consensus is developed among those researchers who have obtained reasonably consistent positive results in testing memory during anesthesia.\(^3\) From this effort would emerge a standard series of readily available tests, stimuli, and methodologies that other investigators could use in their attempts to clarify what happens with memory during anesthesia. A set of standardized test procedures will help to eliminate the file-drawer effect, a fate that might well have befallen the first investigation of Munte et al.\(^2\) if they had not been persistent. We need to be able to place as much confidence in a well-conducted negative study as in the glamorous positive studies.

Studies of memory function during anesthesia ultimately pose the question, what are the differences in explicit and implicit memory? The specer of shadowy memories appearing weeks after an anesthetic event that, in time, develop into true awareness is being raised.\(^4\) If a clear description of an event that is not consciously recalled is given during hypnosis, does it represent explicit or implicit memory?\(^5\) It will be quite some time before we can be sure that the memory effects seen during anesthesia can be categorized as representations of one of the previously described memory systems. Possibly what we are witnessing is the realization that the state of anesthesia may be a perfect tool to catch glimpses of yet another form of memory.

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References