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Memory Retrieval: A Time-Locked Process in Infancy

Abstract. *Three-month-old infants learned to activate an overhead crib mobile by operant footkicking and received a visual reminder of the event (a "reactivation treatment") 2 weeks later, after forgetting had occurred. Subsequent manifestation of the association was a monotonic increasing function of time since the reactivation treatment, and performance of infants tested 8 hours after the reminder was related to the time spent sleeping in the interim* (r = *0.75). These data demonstrate that normal retrieval is time-dependent. Moreover, individual data suggest that retrieval may be continuous rather than discontinuous.*

Most of us have been unable to recall the name of an acquaintance even though we may recall some details of his appearance or the first letter of his name. Later, however, the name may intrude into our thoughts even though we had abandoned our attempt to recall it. This "tip-of-the-tongue" phenomenon is interesting because it demonstrates that a target memory attribute (for example, the name) which is inaccessible for immediate retrieval is nonetheless available in storage. In an early study of this phenomenon (*1*), subjects were given dictionary definitions of infrequently encountered words and asked to name the word. Most who could not said that they knew the word and recalled some of its letters, its number of syllables, the stressed syllable, and words similar to it in meaning or sound. These data are consistent with views (*2*) that memories are collections of independent attributes of an event and that they can be forgotten (or retrieved) at different rates. When cues similar or identical to these memory attributes are subsequently encountered, the memory attributes are presumably aroused, becoming accessible for retrieval. Because attributes that have been aroused will, in turn, activate others that constitute the same memory (*3*), the probability that the target attribute will be aroused and retrieved should improve over hours and perhaps even days. The tip-of-the-tongue phenomenon may be a protracted instance of the normal retrieval process, occurring when insufficient numbers of memory attributes are initially aroused.

Time dependence in normal retrieval has been difficult to demonstrate, probably because retrieval is usually rapid, facilitated by networks of associations constructed and organized by experience. We now report evidence from two studies of human infants that memory retrieval is a time-locked process. We considered 3-month-old infants as ideal subjects for the study of this problem because their facility in learning and remembering a unique association has been well characterized (*4*) and because they lack the verbal facility and extensive experience of older children and adults.

In both studies, infants received two 15-minute training sessions 24 hours apart and a procedurally identical retention test session 13 or 14 days later. During training, infants lay supine in their home cribs with an ankle ribbon connected to one of two overhead suspension hooks. In 9-minute reinforcement periods, the ribbon and a five-object mobile were attached to the same hook, and footkicks produced proportionally vigorous movements in the mobile. In the preceding and following 3-minute nonreinforcement periods, the ribbon and mobile were attached to different hooks so that the mobile, while in view, could not be moved by footkicking. The 3-minute phase at the beginning of session 1 provided an index of the pretraining kick rate; all other nonreinforcement phases were 3-minute cued-recall tests, with the nonmoving mobile components serving as cues for the anticipatory production of footkicking. This training procedure produces a rapid increase in kick rate that is solely attributable to the contingency (*5*). High post-training kick rates persist during cued-recall tests at the beginning of subsequent sessions, with responding gradually declining to the pretraining level over a 2-week period (*4*). This decline in conditioned responding operationally de-

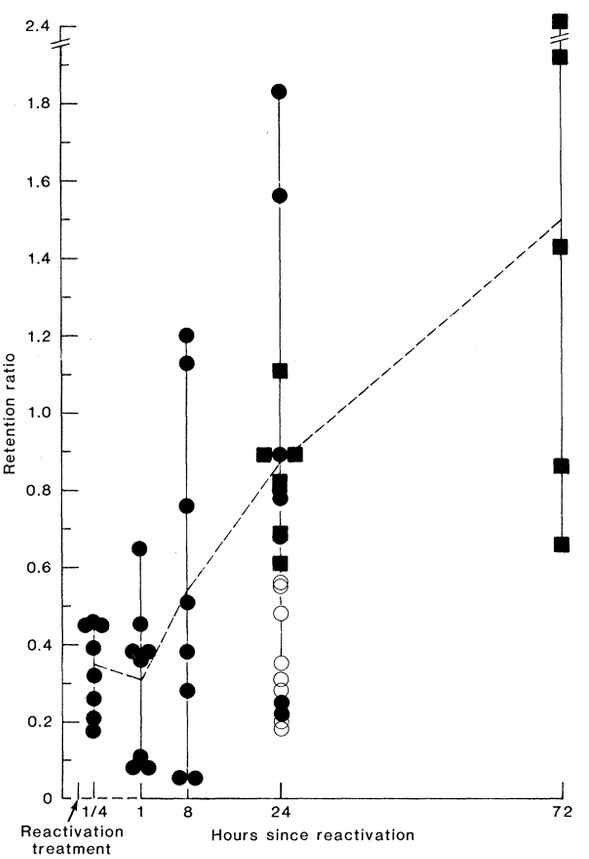

Fig. 1. Retention ratios of 32 infants at different times after a reactivation treatment (filled circles) administered 13 days after the last training session. A ratio of 1.0 indicates no change in performance over the retention interval. Ratios of 8 no-reactivation controls tested after a 14-day retention interval (open circles) and 11 infants, previously tested 24 or 72 hours after a reactivation treatment (filled squares) (*9*), are also shown. Vertical lines define the range of ratios at each delay, and the dashed line connects means for the infants that received the reactivation treatment (filled symbols). The abscissa is not drawn to scale between the reactivation treatment and 1 hour.

fines forgetting. After forgetting is complete, however, it can be alleviated by means of a "reactivation" treatment (*6*) modified from reminder procedures originally developed for use with animals (*7*). The reactivation treatment consists of briefly reexposing the infant to a portion of the original training context (the moving mobile) before the long-term retention test session. Presumably, reencountering these retrieval cues primes available but inaccessible memory attributes such that a sufficient number ultimately becomes accessible.

In past research, the reactivation treatment usually preceded the long-term retention test by 24 hours. This aspect of the procedure originated in animal studies involving shock (the negative reinforcer) as the reminder (*7*) and was continued in infant studies with a moving mobile (the positive reinforcer) as the reminder (*6*). The delay was introduced to permit any unlearned emotional effects of the reminder to dissipate prior to the measurement of learned responding. However, if the normal retrieval process is characterized by the gradual arousal and recruitment of increasing numbers of stored memory attributes, as the tip-of-the-tongue phenomenon suggests, retention more proximal to the reactivation treatment should be measured. We have followed this general approach with appropriate control groups for unlearned effects of the reactivation treatment per se. Retention was measured by dividing an infant's kick rate during the cued-recall test at the beginning of session 3 by its kick rate during the cued-recall test that had immediately followed the completion of training 2 weeks earlier. The resulting retention ratios indexed the proportion of anticipatory responding that persisted after the retention interval. Ratios equal to or greater than 1.00 indicated no forgetting, and those less than 0.40 to 0.50 (depending upon the individual's pretraining rate) indicated no retention. Pearson product-moment correlation coefficients, computed over 150 minutes of paired observations of footkicks by each of two experimenters and an independent observer, were 0.92 and 0.95.

In study 1, 32 infants [mean ($\bar{X}$) age, 83.3 days; standard error (S.E.), 0.76] were randomly assigned to four test groups and received a 3-minute reactivation treatment 13 days after training. The experimental arrangement was the same as during training except that (i) the ribbon was not attached to the ankle but was held by an experimenter, hidden from view, who drew and released it at a rate equal to the infant's kick rate during the last three reinforcement minutes of session 2; and (ii) infants were restrained in a sling seat placed beneath the mobile in their cribs to minimize activity during the reactivation treatment (*6*). These groups received a long-term retention test with the *nonmoving* mobile (the discriminative stimulus) either 1/4, 1, 8, or 24 hours later. In the long-term test, as in the immediate retention test at the conclusion of training, conditioned footkicking was not followed by reinforcement. Four age- and sex-matched reactivation control groups of eight infants each received a rate-matched reactivation treatment and a cued-recall test after corresponding delays but had not been previously trained. These groups provided a baseline of the unlearned effects of the reactivation treatment at different post-reactivation intervals. Finally, two groups of eight infants ($\bar{X}$ age, 88.3 days; S.E., 1.43) were trained for two sessions but received no reactivation treatment before the long-term retention test either 13 or 14 days later. These no-reactivation control groups provided a baseline of forgetting over the retention interval after training.

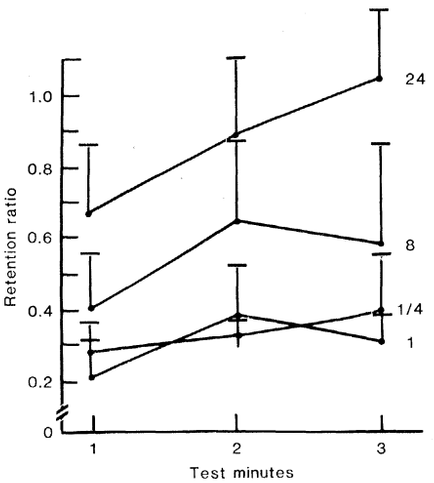

Fig. 2. Mean retention ratios obtained during successive minutes of a cued-recall test administered 1/4, 1, 8, or 24 hours after a reactivation treatment (N = 8 per group). The vertical bars indicate 1 standard error of the mean.

Kick rates of the six training groups did not differ in sessions 1 and 2, with infants learning the association by the second 3-minute block of acquisition [main effect of blocks: $F(4, 240) = 46.26$, $P < 0.001$; Dunnett's t-test: $t(240, 5) = 2.66$, $P < 0.025$]. Thus, subsequent differences in retention between experimental and control groups could not be attributed to differences in original training. Two weeks later, forgetting (as operationally defined) was complete in both no-reactivation control groups; their kick rates during the long-term cued-recall test did not differ from their pretraining baseline rates. Similarly, none of the reactivation control groups exhibited any effects of the reactivation treatment; their kick rates did not differ from those of the no-reactivation control groups. In contrast, retention by groups who had been trained and who had received a reactivation treatment was an increasing monotonic function of time since reactivation [unequal-intervals trend analysis (*8*): $F(1, 28) = 11.06$, $P < 0.001$], with the linear component accounting for 99 percent of the variability among the groups (Fig. 1). Plotting retention ratios of infants previously tested 24 and 72 hours after a reactivation treatment (*9*) yielded a striking description of the time-dependent properties of retrieval (Fig. 1). Figure 2 shows that retention also improves over successive minutes of the cued-recall test [$F(2, 56) = 9.41$, $P < 0.0003$]. This warm-up (*3*) effect apparently sums with the ongoing retrieval process but does not do so differentially with respect to the test group. During reacquisition after the cued-recall test, all groups performed equivalently, confirming that all were physically capable of high response rates in the final session.

To determine whether retrieval was influenced by activity interpolated between the reactivation treatment and the retention test, we asked mothers of infants in the 8-hour test group to record the amount of time their infants slept in that interval. We assumed that external interference would be reduced during sleep, thus allowing greater cognitive effort to be allocated to the retrieval process, increasing its efficiency. The significant correlation ($r = 0.75$, $P < 0.05$) between percentage of sleep during the delay and the retention ratio was consistent with this hypothesis (*10*).

An alternative to the hypothesis that it takes time to "dredge up" forgotten memories is that the infant sling seat introduced novel cues during the reactivation treatment, and these cues interfered with retrieval that would otherwise have been excellent. From this view, the apparent improvement in retention after reactivation would reflect the rate at which the interfering cues were progressively forgotten. In study 2, we tested this possibility by training 16 infants ($\bar{X}$ age, 90.7 days; S.E., 1.55) as before, but administering the reactivation treatment as they lay supine beneath the mobile, as during training and testing. Retention ratios obtained 1 or 24 hours later were the same as those obtained after corresponding delays in study 1. Thus, the improvement in retention as a function

of time since reactivation is not artifactual but reflects a time-locked retrieval process initiated when retrieval cues are noticed during reactivation treatment.

These data raise questions regarding the nature of the retrieval process. Is it a step function or a continuous function? Three aspects of our findings favor the latter: (i) the distribution of individual retention ratios after different delays at each test point (Fig. 1) is rectangular, not bimodal; (ii) progressively higher ratios were attained by infants tested after successively longer delays; and (iii) infants who slept longer during the 8-hour delay had higher retention ratios.

A second question concerns the basis of the reminiscence phenomenon displayed by infants tested after lengthier intervals whose retention ratios exceeded 1.00. We have observed a similar phenomenon after original training: the mean retention ratio peaked at a value greater than 1.00 after a 48-hour delay and significantly exceeded the ratio obtained after only a 24-hour delay (*9*). This phenomenon suggests that the same retrieval process underlies the expression of older (2-week) and younger (2-day) memories.

Third, we must ask what the infants are remembering. Do infants with higher retention ratios remember more about an event (that is, have richer memories)? If attributes are forgotten at different rates, then memories retrieved after different intervals may contain different kinds of attributes (*11*).

Finally, the findings raise questions regarding whether a common, reversible process underlies the actions of reminders and certain amnestic agents that induce progressive forgetting over periods of minutes (for example, electroconvulsive shock) or hours (for example, antimetabolite injection) (*12*).

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How a Nerve Fiber Repairs Its Cut End: Involvement of Phospholipase A_2

Abstract. *Following transection of a giant axon, the nerve membrane at the cut end is resealed within 5 to 30 minutes. This membrane resealing process is highly dependent upon temperature and extracellular calcium ions. The membrane resealing is triggered by excess calcium entering the axoplasm at the site of transection but is prevented by the application of phospholipase A_2 inhibitors. We propose that calcium activated phospholipase A_2 plays a central role in resealing of the ruptured nerve membrane.*

Following transection of a nerve fiber, the proximal cut end regenerates within days to weeks. Before outgrowth and elongation of the proximal cut end the axonal membrane once ruptured must be repaired. It is not known how the cut end of a nerve fiber is resealed or how fast the resealing may occur. As early as 1877, Engelmann showed that the loss of the membrane potential at the injured site of a nerve (demarcation potential) slowly recovers within a few hours (*1*). However, no systematic studies have as yet been made on the membrane resealing process of injured nerve fibers. We have examined the membrane resealing process following transection of the cockroach giant axon, using recovery of changes in the membrane potential and input resistance as criteria. The membrane resealing was found to occur within 5 to 30 minutes after the transection. Our results suggest that the membrane resealing is induced by phospholipase A_2 which is activated by calcium entering at the site of transection.

The cell bodies of the ventral giant axons of the cockroach, *Periplaneta americana*, are located in the sixth abdominal (A_6) ganglion (*2*), and the axons project centripetally through the thoracic ganglia without synaptic interruption. The entire nerve cords and attached ganglia from the first (A_1) through A_6 abdominal segments were excised and placed in a chamber filled with the standard insect saline (*3*). A single giant axon was isolated between the A_4 and A_5 ganglia, leaving its rostral and caudal connections intact. Two microelectrodes were inserted into the isolated axon. While intracellular potentials were recorded from one electrode, the other electrode was used to apply current pulses for measuring the input resistance. The axon was then acutely severed at a point approximately 0.5 to 1.0 mm from the recording site. In order to avoid possible dislodgment of the microelectrodes, the axon was firmly pressed to the bottom of the recording chamber with a broken electrode immediately before cutting. As shown in Fig. 1A, a substantial depolarization was observed at the recording site following the transection. This was accompanied by a drastic decrease in the input resistance, as indicated by potential changes induced by brief hyperpolarizing current pulses applied every 1 minute (Fig. 1A). About 10 minutes later both the resting potential and input resistance recovered to near-normal levels. This behavior is essentially the same as self-resealing of injured cardiac muscle membranes (*4*). The recovery time varied from 5 to 30 minutes in different axons examined at 23° to 27°C. The membrane resealing occurred in the proximal end of the cut distal (terminal side) segment as well as in the distal end of the cut proximal (soma side) segment. Apparently, the resealing that follows immediately after axonal injury is a local event of the nerve membrane and does not depend on the soma (*5*).

The membrane resealing was found to be highly dependent on temperature. Every axon examined above 22°C showed resealing following transection, no resealing occurred below 13°C. This range of temperatures roughly agrees with the phase transition temperatures of membrane lipids (*6*). Because lipids above