Time-Dependent Processes in Memory Storage

Recent studies of learning and memory indicate that memory storage involves time-dependent processes.

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The ability of animals to record experiences and to modify their behavior according to the nature of the experiences clearly ranks as one of the most important as well as one of the most exciting phenomena of biology. In the last decade, and particularly during the last few years, interest in the nature of the processes underlying learning and memory has surged dramatically. To a considerable degree research into the physiological bases of memory has consisted of attempts to find evidence of some permanent change in neural functioning produced by experience.

Although there is increasing evidence that experiences do in fact produce relatively long-lasting neural changes (*1*), clear evidence of specific changes produced by specific experiences has so far eluded even the most imaginative researchers. The problem of the basis or bases of memory would be much easier to solve if neural functioning and behavior were less plastic than they have been found to be. It has been known for many years that learning does not consist simply of acquiring tendencies to make specific responses in the presence of particular stimuli. Most animals can readily demonstrate retention of an experience by performing in a variety of ways in the presence of complex and varied stimulation (*2, 3*). "Fixation of memory" is clearly *not* synonymous with fixation of behavior. As far as behavior is concerned, memory is not only the capacity to repeat, it is the capacity to vary. This simple fact of behavior has for many years provided serious difficulties for theoretical speculations concerning the nature of the processes underlying memory.

A complete theory of memory must not only encompass this embarrassing fact but also handle the complicated problem of memory trace consolidation. It is becoming increasingly clear, on the basis of recent research findings, that the memory trace of an experience is not laid down in any lasting way either during or immediately after the experience. Rather, it appears that short-term processes provide a temporary basis for recall of experiences and that the consolidation of long-term traces involves processes occurring over relatively long intervals of time. It seems likely that an understanding of memory trace consolidation processes will provide important clues to the nature of long-term storage and retrieval processes. For these reasons the problem of memory trace consolidation is currently the focus of research in numerous laboratories. In this article I review some of the findings of recent studies concerned with this problem. In the first sections I review evidence that memory trace consolidation can be influenced—either impaired or enhanced—by a variety of treatments. In the final section I discuss some recent behavioral evidence concerning time-dependent effects in memory storage.

Experimental Analysis of Retrograde Amnesia

The most extensive evidence concerning memory consolidation has come from studies of experimentally induced amnesia. It has been known for many years that human patients who have suffered head injuries tend to have difficulty recalling events that occurred shortly before the injury even though older memories may be completely intact (*4*). This selective loss for recent memory, termed "retrograde amnesia," has also been observed in patients given electroshock treatments (*5*). Systematic experimental studies of retrograde amnesia in infrahuman species were initiated almost 20 years ago, but the theoretical and methodological questions raised by the initial experiments are currently active issues. In the first of such experiments (*6*), animals were given an electroconvulsive shock (ECS) after each trial in a learning task. Animals given electroshock immediately after each training trial showed little evidence of learning. In general, learning rate increased directly with increases in the interval between learning trial and treatment. Since electroshock produces—at least momentarily—profound electrophysiological disturbances in the brain, these experiments, as well as numerous similar ones (*7*), provided strong evidence for the general hypothesis that memory trace consolidation processes are time-dependent. However, the experiments did not completely rule out the possibility that the results were due to some other effect or effects of electroshock. For example, it was suggested that punishment, rather than amnesia, might be the basis of the retrograde effect of electroshock treatments (*8*). That is, since electroshock was administered immediately after each training trial, it seemed at least possible that the animals were merely learning to avoid making the responses that were followed by the electroshock treatment. According to this view, the failure of animals to perform under such conditions is not due to a memory loss.

Recent evidence does not support this alternative view of the basis of electroshock effects. In one experiment in our laboratory, for example (*9*), rats were placed on a small platform and were given a mild shock to the feet as they stepped from the platform onto the floor. Half the animals were given electroshock within a few seconds. On a retention test given the next day, the rats given only the foot shock tended to remain on the platform—that is, they appeared to remember the shock—while those given electroshock after the foot shock gave no evidence of remembering either the foot shock or the electroshock. They readily stepped off of the platform. In subsequent experiments my associates and I, as well as other investigators, have made extensive use of one-trial

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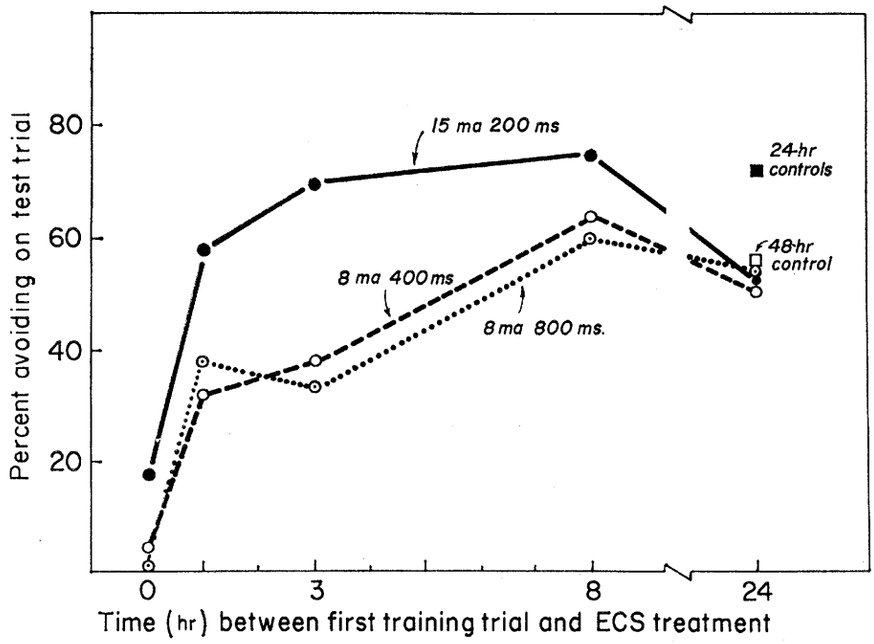

Fig. 1. The effect of duration of electroshock stimulation on retrograde amnesia. With durations of 400 or 800 milliseconds, amnesia is observed when electroshock is administered as long as 3 hours after a single training trial on an inhibitory avoidance learning task. The 24-hour and 48-hour controls did not receive electroshock. [McGaugh and Alpern (*34*)]

inhibitory learning tasks (or so-called "passive avoidance") in studies of memory consolidation.

In other experiments we have found that electroshock treatments are aversive if they are given repeatedly. Rats can learn to avoid making responses that are repeatedly followed by electroshock, and they can learn to avoid going to a place in a maze where they have received several electroshock treatments (*10*). However, in all of our experiments, aversive or punishing effects were observed only after *several* electroshock treatments had been administered, while retrograde amnesia was readily obtained with a single treatment. Thus, the amnesic effects of a single electroshock treatment cannot be interpreted in terms of punishing effects. Other investigators have shown that the amnesic effect of a single treatment is independent of the place (the training apparatus, home cage, and so on) in which the treatment is given (*11, 12*). It seems clear then that electroshock treatments can produce retrograde amnesia, and it seems highly likely that the amnesia is produced directly by the electroshock stimulation. Recent results support this view. The convulsion usually produced by electroshock stimulation seems to be unnecessary for the occurrence of amnesia. In an experiment in our laboratory (*13*), mice were placed one at a time on a small platform attached to the side of a box and were allowed to enter the box through a small hole. Each mouse received a foot shock as it entered. The mice were then given light ether anesthesia, electroshock, or electroshock stimulation delivered while the animals were anesthetized with ether. The ether anesthesia prevented the electroshock convulsions. On a retention test trial the following day, animals in groups given, 25 seconds after the foot shock, either a typical electroshock treatment or electroshock stimulation while anesthetized, showed little evidence of remembering the shock. For both of these groups, the percentage of mice remaining (for over 10 seconds) on the platform on the retention trial was significantly lower than the percentage for the other groups. In this experiment the ether anesthesia produced no amnesia.

The findings of the experiment just discussed also indicated that the electroshock stimulation did not significantly affect performance when it was administered 1 hour after the training trial. In other research we have found that the magnitude of the retrograde amnesic effects of electroshock depends upon the duration of the electroshock stimulation. The intensity of the current seems not to be important so long as it is sufficient to elicit convulsions in unanesthetized animals. The standard duration in most experiments, including the one just described, is 200 milliseconds. With the 200-millisecond treatment, we have generally obtained a relatively steep gradient with relatively little amnesia when electroshock is administered more than 30 minutes after training. Some investigators have reported even steeper gradients of retrograde amnesia with little or no amnesia when more than a minute elapses between the training trial and the electroshock treatment (*12, 14*). In recent experiments (Fig. 1) we have produced retrograde amnesia in mice with intervals between training and treatment as great as 3 hours when the duration of the electroshock stimulation was increased to 400 or 800 milliseconds (*15*). These results suggest that it should be profitable to study the differential effects of electroshock stimulation of differing duration on brain electrophysiological activity. We have just started to work on this problem, and initial findings indicate that different durations of electroshock stimulation have markedly different effects on electrophysiological activity of the brains of mice.

In a general way, the findings of studies of the effects of electroshock stimulation are highly similar to results obtained with other treatments which have been found to produce retrograde amnesia. A number of investigators have reported that deep anesthesia can produce retrograde amnesia. The duration of the temporal gradient has been found to differ considerably with different treatments. When a relatively simple learning task is used, deep ether anesthesia produces amnesic effects only if the ether is administered within a few seconds of the task, while with pentobarbital, significant effects are found with intervals between training and treatment of as much as 10 minutes (*16*). With a highly complex task (successive discrimination learning), we have found evidence of amnesic effects of barbiturates even when the drug (pentobarbital sodium or Brevital sodium) was administered several hours after training (*17*).

Investigators in several laboratories have reported that retrograde amnesia can be produced by inducing "spreading depression." Topical application of potassium chloride (*18*) to the cerebral cortex produces a depression of electrical activity which spreads across the cortex of the treated hemisphere and results in a temporary inhibition of functioning of the affected cortex. In a study by Ray and Emley, rats were

first trained on a visual discrimination task a few minutes after unilateral spreading cortical depression was induced with potassium chloride. No evidence of memory was found when the rats were tested with the opposite hemisphere depressed. Memory storage during the original training was clearly restricted to the untreated hemisphere. The animals were then given a single "training-transfer" trial with neither cortex depressed, and then, either 15 seconds or 10 minutes later, potassium chloride was applied to the "trained" cortex (that is, the cortex which was not depressed during original training). On retention test trials given 30 minutes later, the group treated with potassium chloride 10 minutes after the single "transfer" trial performed perfectly, whereas no evidence of memory was found in the group treated 15 seconds after the "transfer" trial. A single experience appears to be sufficient for bilateral replication of memory storage processes originally located unilaterally. But this transfer process, like that involved in original learning, appears to be time-dependent. Albert (*19*) has reported that even greater amnesic effects are found when potassium chloride is applied to the "naive" or "receiving" cortex within 2 hours after a single "transfer" trial with neither cortex depressed. These findings suggest that the time required for initial transfer of a replicated trace from one hemisphere to another is considerably shorter than that required for the complete fixation of the replicated trace in the previously "naive" hemisphere. Of further interest is the finding that the magnitude of the amnesic effect found with potassium chloride treatments is a function of the duration of the treatment. With long (up to 30 minutes) potassium chloride treatments, the degree of retrograde amnesia obtained is roughly comparable to that we have found with 800-millisecond electroshock stimulation.

Other recent research findings indicate that memory consolidation in mice and goldfish is impaired by intracranial injections of the protein synthesis inhibitor, puromycin (*20, 21*). Agranoff *et al.* (*21*) have reported that puromycin injected prior to training does not impair acquisition of an avoidance response but does impair retention of the response, as observed when animals are tested several days later without further drug treatments. Retention is also impaired if the compound is injected after training, but only if the injections are given within an hour of training. Thus, puromycin seems to act selectively on memory consolidation. With either pre- or posttraining injections, the degree of impairment of retention increases directly with increases in the dose of puromycin injected. This finding is interesting in view of evidence that the duration of protein synthesis inhibition varies directly with the dose of puromycin. As Agranoff and his associates point out, the behavioral and biochemical findings are not completely consistent. For example, a dose of 90 milligrams of puromycin injected prior to training does not impair memory consolidation 1 hour after the injection even though evidence indicates that this dose of puromycin inhibits protein synthesis for at least 2 hours following administration. Also, under some conditions, the amnesic effects of electroshock appear to be greater than those of puromycin.

Although it seems clear, on the basis of this evidence, that memory consolidation is impaired by puromycin, it has not yet been demonstrated either that the impairment of memory consolidation is due solely to impairment of protein synthesis or that inhibition of protein synthesis is essential for impairment of memory consolidation. It is highly likely that protein synthesis is in some way involved in long-term memory consolidation.

These recent findings of experimental studies of retrograde amnesia provide very strong evidence that long-term memory trace consolidation processes are time-dependent. The findings have not as yet, however, provided an understanding of the nature of the processes involved in the consolidation of durable memory traces. In particular, it is not known whether the effects of the various treatments discussed above have a common physiological basis or whether the common effect—retrograde amnesia—is produced by a number of different mechanisms. The problem is amenable to analysis, however, and the results of research currently in progress in several laboratories will in all probability help to clarify these issues.

Drug Facilitation of Learning and Memory

There is little doubt that memory storage can be impaired. There is also accumulating evidence that memory storage can be facilitated. Several years ago Lewis Petrinovich and I initiated a series of studies of the effects of central-nervous-system stimulants on learning. We were guided initially by a "discovery" of Lashley's early report that maze learning in rats was facilitated by administration of low doses of strychnine sulfate (*22*). In several experiments we, as well as others, have obtained additional evidence that strychnine facilitates learning (*23*). Petrinovich and I found, for example, that injection of low doses of strychnine sulfate prior to training trials enhanced rats' learning of an alley maze. Subsequently we found that strychnine injections facilitated learning of other tasks, including discrimination learning. The results of one experiment are shown in Fig. 2. Rats were injected with strychnine sulfate a few minutes before they were given massed training trials on a visual discrimination problem, with foot-shock motivation. As may be seen, the strychnine-injected animals learned to meet a criterion with fewer trials and errors than the controls did. These results, as well as those of other studies, suggest that strychnine may facilitate processes underlying learning of the task. Other interpretations of the results of these experiments, including interpretations stressing possible motivational effects of the drug, could not be readily excluded, however.

Recent experimental findings have provided strong evidence that central-nervous-system stimulants can facilitate learning by enhancing memory consolidation. In several experiments we, and subsequently others (*24, 25*), have found that the learning of a variety of tasks in rats and mice is facilitated by injection of strychnine shortly *after* training trials. No facilitation is obtained however if the strychnine is administered more than 30 minutes after the training is terminated. In most of these experiments, retention tests were given at least 23 hours after the injections; the animals were never tested while drugged. Consequently the posttrial injection studies are difficult to interpret in terms of motivational or perceptual effects. Similar facilitating effects of posttrial administration of drugs have been obtained with a number of central-nervous-system stimulants. Figure 3 shows the results of a study of the effect of posttrial injections of picrotoxin on maze learning. Rats in this experiment were given either saline or one of several doses of picrotoxin immediately after each daily trial in a com-

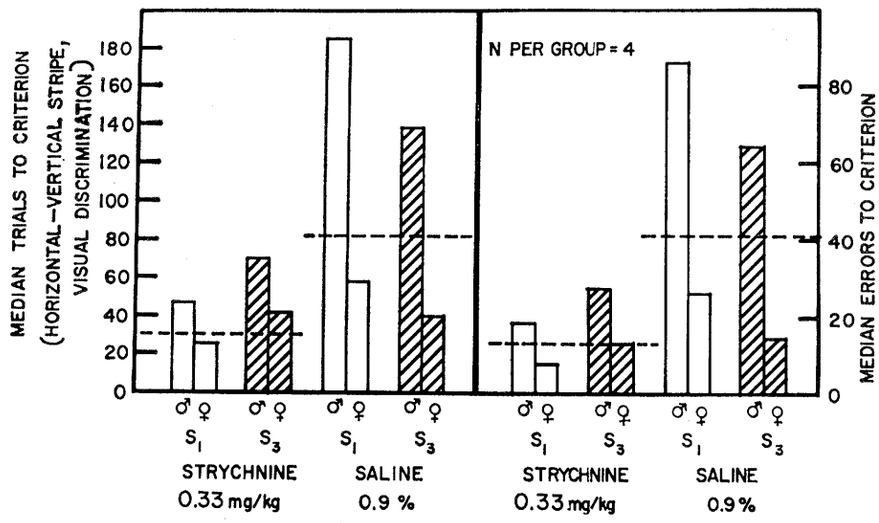

Fig. 2. The effect of strychnine sulfate on simultaneous discrimination learning in two strains of rats. The animals were injected prior to massed training trials. Horizontal dashed lines indicate overall medians for strychnine-injected and control (saline-injected) animals. [Based on findings of McGaugh and Thomson (*35*)]

plex maze. In both strains tested, but particularly in the S_3 strain, errors decreased with increases in the dose of picrotoxin. Recently Hunt and Krivanek (*24*) reported that rats' learning of a variety of tasks is facilitated by either pre- or posttrial injections of Metrazol (pentylenetetrazol). We have confirmed this finding in several experiments. Figure 4 shows the results of one of our experiments. Mice of two strains were injected with either saline or one of three doses of Metrazol immediately after each daily trial in a Lashley III alley maze. As Fig. 4 shows, facilitation was found with both strains, but the most effective dose was found to differ for animals of the two strains. In most, but not all, of our experiments with central-nervous-systems stimulants, we have found significant strain differences in dose-response effects.

In several experiments we studied the effect of the synthetic strychnine-like compound 5,7-diphenyl-1,3-diazaadamantan-6-ol (1757 I.S.) on learning and memory storage. Clearly facilitating effects have been found with both pretrial and posttrial injections. Figure 5 summarizes the results of one experiment. Food- and water-deprived rats were injected with either 1757 I.S. or a control solution each day for 5 days immediately after each trial in a maze. Half of the animals were rewarded on each trial and half were not. Following the fifth and each of five succeeding trials, all the animals were rewarded and all were given only control injections. Figure 5 shows that results for the nonrewarded drug-injected and control groups did not differ on trials 2 through 5. Results for the two rewarded groups did differ on trials 2 through 5: the animals given 1757 I.S. made significantly fewer errors. On trials 6 through 10 both groups previously given 1757 I.S. made fewer errors than the two control groups. These results suggest that 1757 I.S. facilitated the "latent" learning occurring during nonrewarded trials as well as conventional maze learning. Again, the effects appear to be due to enhanced consolidation of memory.

The list of drugs found to facilitate learning in laboratory animals continues to grow. Recently learning facilitation has been found, for example, with pretrial injections of amphetamine, nicotine, and magnesium pemoline (*26*). Facilitation of learning has also been found with posttrial injections of caffeine, physostigmine, and amphetamine (*27*).

Considered together, these recent findings provide strong evidence that learning can be facilitated by drugs and that drugs can affect learning in several ways. Some of the drugs studied seem to improve performance by enhancing attentional or short-term memory processes, or both. Posttrial injections of nicotine, for example, seem not to affect learning (*28*). Other drugs seem to enhance posttrial memory storage processes. An understanding of the nature of these drugs' effects on central-nervous-system processes could provide important clues to memory storage. However, each drug has diverse and complex effects on central-nervous-system activity. It may be that the various drugs do not have a common mechanism of action and that they affect memory storage in different ways. At a more general level it would be of interest to know whether the drugs which enhance memory when administered afer training can either pre-

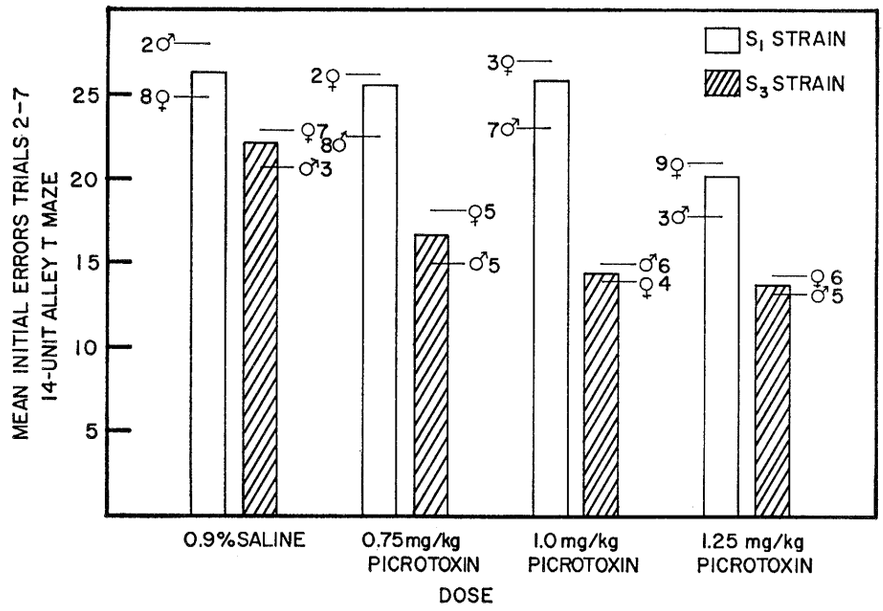

Fig. 3. The effect of picrotoxin on maze learning in two strains of rats. The rats were injected immediately after each daily trial. Horizontal lines indicate means for males and females in each group; numbers indicate number of animals in each subgroup. [Based on findings of Breen and McGaugh (*36*)]

vent or attenuate retrograde amnesia produced by electroshock treatments. Such evidence would strengthen the interpretation that the drugs enhance memory consolidation. In a number of unpublished studies (*29*), rats have been injected with central-nervous-system stimulants prior to training and given an electroshock several minutes after training. In general the results of retention tests given later suggest that the drugs attenuate but do not prevent electroshock-induced retrograde amnesia; however, the findings have not been consistent, and more research on this problem is needed. The fact that most of the drugs investigated potentiate the convulsive effects of electroshock makes the results of this type of experiment difficult to interpret. The hypothesis that the drugs facilitate memory by enhancing consolidation does not necessarily imply that the drugs should prevent retrograde amnesia. It may be, for example, that the drugs increase the duration of consolidation processes without increasing the rate at which consolidation occurs. According to this interpretation, it might be possible to prevent posttrial facilitating effects of central-nervous-system stimulants on learning by administering electroshock to animals at just the time after training at which it produces little or no amnesia in control animals. This possibility has not yet been investigated.

Time and Repetition Effects in Memory Storage

Overall, the evidence from studies of the effects on memory of electroshock and drugs clearly indicates that memory trace consolidation involves processes which are time-dependent. There is also a considerable amount of purely behavioral evidence that memory storage is time-dependent (*30*). Recently Alpern and I conducted a series of behavioral studies of retention in mice to see if retention at various intervals following one or more training trials varies systematically with the time between training and retention testing. To investigate this problem, we first gave mice a single training trial on the inhibitory avoidance task described above (see *13*) and a retention test either 5 seconds, 30 seconds, 2 minutes, 1 hour, or 24 hours later. As may be seen in Fig. 6 (middle curve), for intervals up to 2 minutes, retention in-

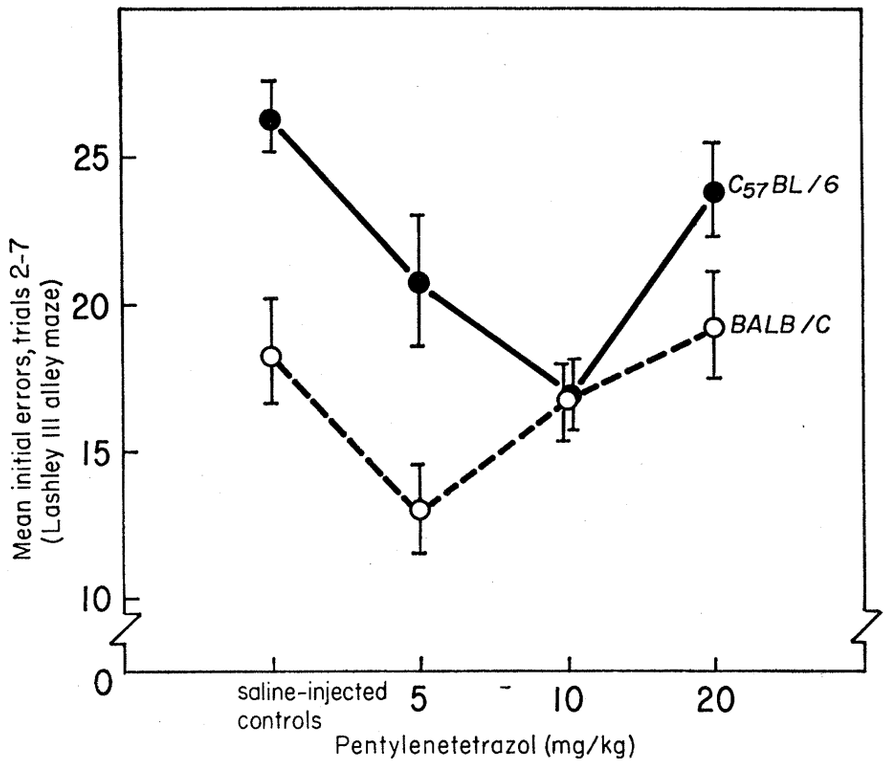

Fig. 4. The effect of Metrazol (pentylenetetrazol) on maze learning in two strains of mice. The mice were given an injection after each daily trial. Vertical lines indicate standard error of ± 1. [McGaugh (*37*)]

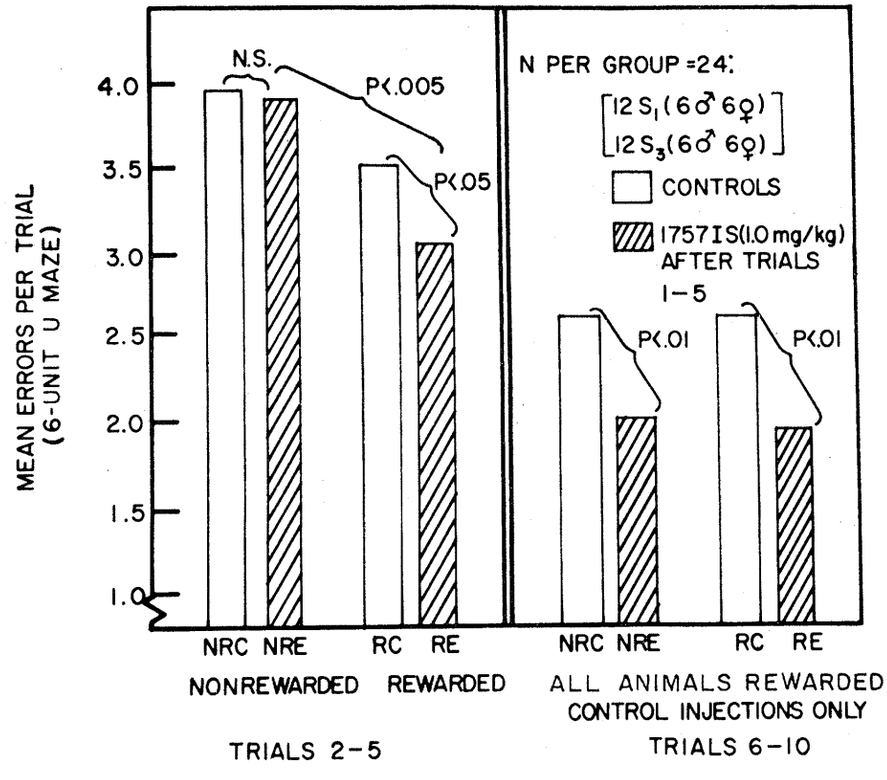

Fig. 5. The effect of 5,7-diphenyl-1,3-diazaadamantan-6-ol (1757 I.S.) on maze learning in rats. (*NR*) Nonrewarded; (*R*) rewarded; (*E*) 1757 I.S. injected after each daily trial for 5 days; (*C*) control (citrate buffer) injection given after each trial. Facilitation found on trials 6 to 10 was independent of reward condition during the first five trials. [Based on data of Westbrook and McGaugh (*38*)]

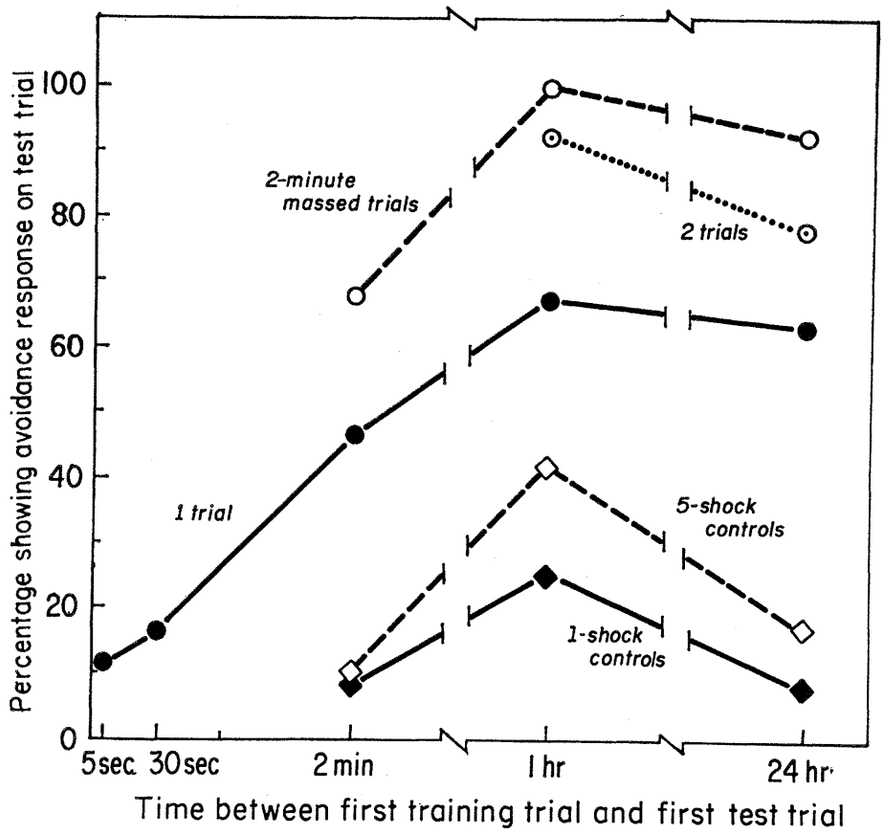

Fig. 6. Retention of inhibitory avoidance (step-through task) (see *13*) as a function of time and number of training trials given during the first 2 minutes of training. Retention (that is, percentage of mice showing avoidance response on retention test) after a single trial increases with increase in the interval between the training and test trials (middle curve). Retention is enhanced by repetition of trials. The two lower curves show that the retention performance is not due to a nonspecific effect of foot shock; animals in the groups represented by the lower curves were given foot shocks in a different apparatus and then tested on the step-through apparatus at one of the times indicated. [McGaugh and Alpern (*15*)]

creased as the time between the training trial and the retention trial was increased. No significant retention was found for the 5-second and 30-second intervals. Over the intervals tested, retention does appear to be time-dependent. These results caused us to wonder whether the rate of increase in retention within a 2-minute period was completely time-dependent or whether the retention could be improved by giving the mice additional training trials during the 2-minute interval. To answer this question, we gave mice massed training trials on the step-through task for 2 minutes. As Fig. 6 shows, the performance of these animals (top dashed curve) on the last training trial (that is, at 2 minutes) was superior to that of animals given a single trial. Improvement in performance over the 2-minute period appears to be both time- and event-dependent. Other results shown in Fig. 6 indicate that the performance, on delayed retention tests, of mice given either two trials (the second trial 2 minutes after the first—dotted curve) or massed training trials for 2 minutes (top curve) was also superior to the performance of those given only one trial (middle curve). To provide a control for possible nonspecific effects of the foot shock punishment, control mice were given foot shock in a different apparatus and then tested on the step-through apparatus. Although there were some increases in latency found with this procedure (Fig. 6, bottom curves), it is clear that the latencies of the trained animals were not due simply to the fact that they had received foot shock.

Retention in this task increases with both time and number of trials. But do the increases in retention directly reflect memory consolidation processes? In an attempt to answer this question we gave mice a single electroshock treatment (8 milliamperes, 800 milliseconds) either 2 minutes or 1 hour after the first trial on the step-through apparatus. Different groups were given either one trial, two trials, or massed training trials during the first 2 minutes. All the animals were given a single retention test the next day. For purposes of comparison, other groups were given a single trial followed by an electroshock treatment 5 seconds or 24 hours later. As Fig. 7 shows (solid curve), the group given electroshock 5 seconds after the trial showed no retention, and the group shocked 24 hours after the trial showed no impairment of retention (relative to retention for a control group which received a single training trial followed by a single retention trial after 48 hours). The effect of the number of training trials varied with the time of administration of electroshock. When electroshock was administered 2 minutes after the first training trial, retention 24 hours later did not vary significantly with the number of training trials. The number of training trials did affect retention, however, when electroshock was given 1 hour after training. The retention of animals given two or more training trials was significantly better than that of animals given in single trial.

A comparison of the results of Fig. 6 with those of Fig. 7 shows that increases in retention found with increases in time do not depend solely upon consolidation processes as indexed by electroshock effects. For all intervals up to 1 hour that were investigated, the performance of animals *tested* at the end of the interval in question was superior to that of comparably trained animals given an electroshock at the end of that interval and a retention test the following day. This effect is seen most clearly in the one-trial groups. When tested at 1 hour after training (Fig. 6), 68 percent of the animals in the one-trial group remained on the platform. When animals were given electroshock 1 hour after training and a single retention trial the next day, only 28 percent remained on the platform. During the first few hours after training, memory seems to be based, at least in part, on processes other than those involved in long-term storage.

In another experiment we studied the effect on memory storage of a single additional training trial given 1 hour after previous single and multiple trials. As Fig. 8 shows, when only one original training trial was given, a single additional trial given 1 hour later significantly increased avoidance in tests

made the next day. Electroshock attenuated the effect of the additional trial. If the animals were given an electroshock immediately after the additional trial, their performance 24 hours later was similar to that of animals given neither an additional trial nor an electroshock. Each training trial, whether given early or later in training, initiates memory storage processes that are time-dependent.

Conclusions

These observations indicate that the long-lasting trace of an experience is not completely fixed, consolidated, or coded at the time of the experience. Consolidation requires time, and under at least some circumstances the processes of consolidation appear to be susceptible to a variety of influences—both facilitating and impairing—for several hours after the experience. There must be, it seems, more than one kind of memory trace process (*31*). If permanent memory traces consolidate slowly over time, then other processes must provide a temporary basis for memory while consolidation is occurring. The evidence clearly indicates that trial-to-trial improvement, or learning, in animals cannot be based completely on permanent memory storage. Amnesia can be produced by electroshock and drugs even if the animals are given the treatment long after they have demonstrated "learning" of the task.

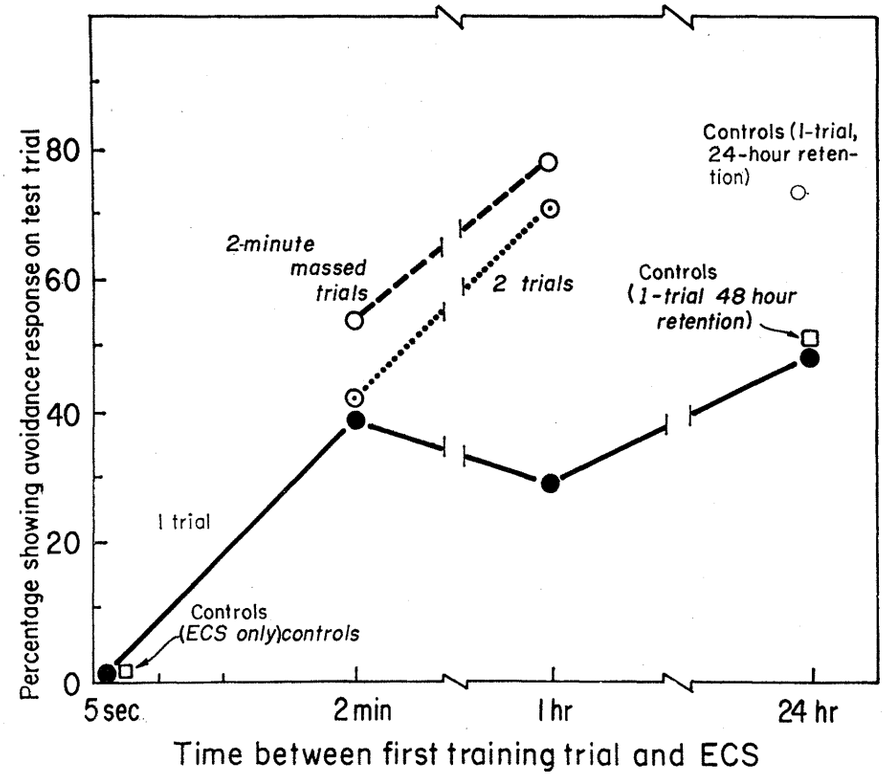

Fig. 7. The effect of electroshock (8 milliamperes, 800 milliseconds) on retention of an inhibitory avoidance response. The lower curve shows that the effect of electroshock decreased as the time between a single training trial and the electroshock treatment was increased (this is also shown in Fig. 1). The two upper curves show that the effect of electroshock given 1 hour after training was attenuated by increasing the number of training trials during the first 2 minutes of training. The retention trials were given 24 hours after training for all groups except for the 48-hour controls. As may be seen, the performance (50 percent) of this control group was poorer than that (63 percent) of the 24-hour-retention group shown in Fig. 6. Thus for all groups given electroshock, with the exception of the 24-hour group, performance on the 24-hour retention test was lower than that of controls on the 24-hour retention test (see Fig. 6). The controls were given electroshock only and received no foot shock. [McGaugh and Alpern (*34*)]

Of particular interest is the finding that retention of the inhibitory avoidance response increases with time. In a sense this should be expected, for it has long been known (and ignored) that, within limits, learning is facilitated by increasing the interval between repeated trials (*7, 30*). Our result may be the simplest case of such an effect. Since the improvement in retention with time seemed not to be due solely to consolidation (as indicated by electroshock effects), it would seem that the "distribution of practice" effect, as it is typically designated, may be due in part to a time-dependent *temporary* memory storage process. In our work with animals we have found no analog of human immediate memory such as that required for repeating digits (or finishing sentences). Animals tested immediately on the task described above after a trial typically showed no evidence of memory. It could be that the poor performance is due to excessive fright, but the "distribution of practice effect" is also typically observed in learning experiments in which food reward is used rather than shock avoidance. Since the retention tasks require the animals to change their behavior in some way, it could well be that the growth of retention over the first few minutes after a trial is due to time-dependent processes involved in the organization of processes necessary for changing behavior, in addition to those involved in temporary storage and retrieval. It is worth pointing out that there is evidence of an analogous process in human memory (*32*).

A complex picture of memory storage is emerging. There may be three memory trace systems: one for immediate memory (and not studied in our laboratory); one for short-term memory which develops within a few seconds or minutes and lasts for several hours; and one which consolidates slowly and is relatively permanent. The nature of the durability of the long-term memory trace (that is, the nature and basis of forgetting) is a separate but important issue. There is increasing evidence and speculation (*20, 21, 33*) that memory storage requires a "tri-trace" system, and our findings are at least consistent with such a view.

If there are, as seems possible, at least three kinds of traces involved in memory storage, how are they related? Is permanent memory produced by activity of temporary traces (*31*), or are the trace systems relatively independent? Although available findings do not provide an answer to this question, there does seem to be increasing evidence that the systems are independent. Acquisition can occur, as we have seen, without permanent consolidation, and both short-term and long-term memory increase with time. All this evidence suggests (but obviously does not prove) that *each* experience triggers activity in *each* memory

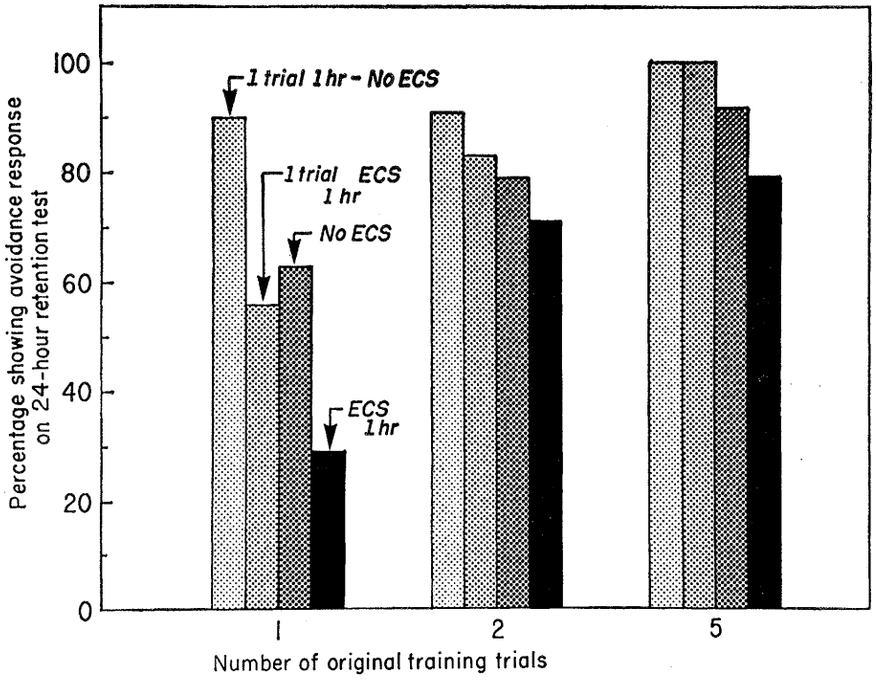

Fig. 8. The effect of an additional training trial 1 hour after the original training trial or trials (given during the first 2 minutes of training) on 24-hour retention of an inhibitory avoidance response. In groups given a single original training trial, a single repetition significantly enhanced retention. A single electroshock administered after the additional trial attenuated the effect of the trial on subsequent retention. The effects of the additional training trial as well as the effects of electroshock decreased as the number of original training trials was increased. [McGaugh and Alpern (*34*)]

system. Each repeated training trial may, according to this view, potentiate short-term processes underlying acquisition while simultaneously enhancing independent underlying long-term consolidation. Obviously, acceptance of these conclusions will require additional research.

If this view is substantially correct, it seems clear that any search for *the* engram or *the* basis of memory is not going to be successful. Recognition of the possibility that several independent processes may be involved at different stages of memory may help to organize the search. A careful examination of the time course of retention and memory trace consolidation, as well as examination of the bases of the effects of memory-impairing and memory-facilitating treatments, may help to guide the search. It is clear that a complete theory of memory storage must eventually provide an understanding of time-dependent processes in memory.

In 1930 Lashley wrote (*2*), "The facts of both psychology and neurology show a degree of plasticity, of organization, and of adaptation and behavior which is far beyond any present possibility of explanation." Although this conclusion is still valid, the current surge of interest in memory storage offers hope that this conclusion may soon need to be modified.

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