Effects of Electroshock on Memory: Amnesia without Convulsions

Abstract. *Mice received a single training trial on an inhibitory avoidance task and a retention trial 24 hours later. Electroshock stimulation, administered 25 seconds after the training trial, produced amnesia even if the convulsion was prevented by ether anesthesia. The amnesia produced by such shock is apparently due to the electric current and not to the convulsion.*

Investigators of time-dependent processes in memory storage have made extensive use of electroconvulsive shock (ECS) as a technique for producing retrograde amnesia. A single such ECS produces amnesia for events that occur shortly before the treatment (*1*). The general interpretation of this finding has been that electroshock current interferes with relatively long-lasting processes underlying memory storage. Overall, the evidence is highly consistent with this interpretation (*2*). Other interpretations have stressed the possibility that the behavioral effects are due to the convulsions rather than to the current (*3*). The effects produced by a *series* of shock treatments (for example, attenuation of a conditioned emotional response; aversive and disruptive effects) do, in fact, seem to be due to the convulsions. The disrupting effects of a series of shocks are not obtained if the shocks are administered while the animals are under ether anesthesia (*4*); the anesthesia prevents both the convulsions and the behavioral effects.

We have now investigated the amnesic effects of single electroshocks administered to mice under ether anesthesia. Our findings indicate that elicitation of a convulsion is not a necessary condition for the production of amnesia. Our evidence strengthens the idea that electroconvulsive shock produces retrograde amnesia by direct interference with processes of memory storage.

Two hundred Swiss-Webster mice (60 to 70 days old) were used as subjects. All animals were given two trials, separated by 24 hours, on an inhibitory, avoidance-learning task (*5*). On each trial a mouse was placed on a small (2.25 by 6.25 cm) metal platform extending from the outside wall of a box and directly in front of a hole (3.75 cm in diameter) leading to the darkened interior of the box. A 40-watt bulb was located 19 cm above the platform. The apparatus was placed on the edge of a table so that the platform was approximately 1 m from the floor of the room. All mice were given one "training" trial and one retention test trial 24 hours later. On each trial the time the mouse spent on the platform before it stepped into the box was recorded.

The mice were divided into ten groups, each with ten males and ten females. The treatments given the different groups are shown in Fig. 1. Mice in the six groups shown on the left received a footshock of approximately 3 ma as they stepped from the small platform into the box. The controls received no other treatment.

The "ether" animals were placed in a desiccator that contained cotton saturated with approximately 10 ml of diethyl ether immediately after the trial and were removed 25 seconds later. The anesthesia was sufficient to cause loss of consciousness (as indicated by complete ataxia) for approximately 1 minute. Two groups were given electroshocks 1 hour after the trial. Mice in one of these groups were anesthetized prior to stimulation and were completely anesthetized at the time shock was administered. Two other groups were given electroshock 25 seconds after the training trial; one of these groups was anesthetized with ether before stimulation. The electroshock consisted of a current of approximately 20 ma, delivered for 200 msec, by way of corneal electrodes. During electroshock stimulation the mouse was held in the experimenter's hand. The shock elicited tonic convulsions, with full leg extension, in all unanesthetized mice. The current elicited only a slight and brief twitch in the anesthetized mice.

Four groups (shown on the right side of Fig. 1) did *not* receive foot shock as they stepped into the box on the first trial. The controls received no treatment. One group was anesthetized for 25 seconds. Another group was anesthetized for 25 seconds and then given electroshock. The fourth group was given electroshock 25 seconds after the trial. These four groups served as controls for possible effects of ether and shock when administered without prior foot shock (*6*).

On the first trial the median step-through latency was 2 seconds. Ninety-six percent of the mice entered the box in less than 10 seconds. Figure 1 shows the percentage of mice in each group remaining on the platform for 10 seconds or longer on the 24-hour retention test. This criterion was attained by over 50 percent of the mice in four of the groups given foot shock on the first trial: controls (foot shock only); ether; ECS at 1 hour; ether and ECS at 1 hour. The differences among the four groups did not approach statistical significance ($H = 2.42$, $df = 3$, $p > .05$; Kruskal-Wallis test). Thus, no amnesia was found with ether, delayed ECS, or delayed ECS administered during ether anesthesia (*7*). The results shown on the right in Fig. 1 indicate that the ether and ECS treatments did not affect the second

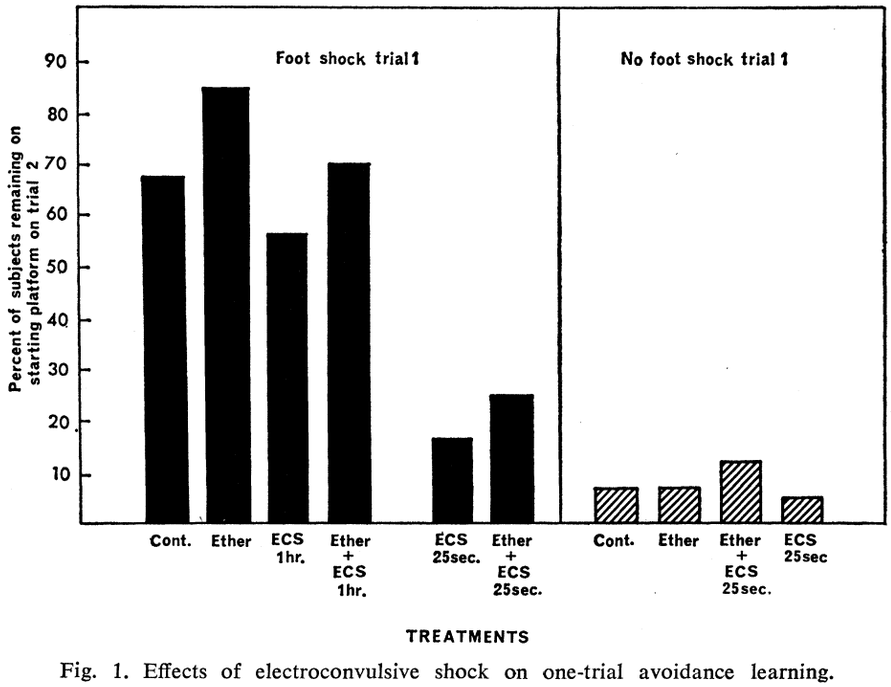

Fig. 1. Effects of electroconvulsive shock on one-trial avoidance learning.

trial latencies of mice which were not given foot shock on the first trial.

The results obtained for the two groups of mice given electroshock 25 seconds after the foot-shock indicate that electroshock produced amnesia even when it was administered while the animals were anesthetized. The latencies of the two groups were similar; for both groups they differed significantly from those of all the other four foot-shocked groups ($p < .01$), but they did not differ significantly from those of the four groups which were not given foot shock on the first trial ($H = 8.03$, $df = 5$, $p > .05$).

These results indicate quite clearly that the retrograde amnesia produced by electroshock is due to the current and does not depend upon the elicitation of a behavioral convulsion. The findings are, of course, completely inconsistent with the suggestion that the retrograde effect of electroconvulsive shock is due to conditioning of competing responses which are elicited by the shock (*3*). The findings of this study are consistent with other evidence (*8*) that prevention of tonic convulsions does not attenuate retrograde amnesia induced by electroconvulsive shock. Subsequent attempts to understand the basis of the amnesic effect of such shocks should focus on the neurophysiological and biochemical effects of electroshock stimulation.

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References and Notes

1. D. J. Leonard and A. Zavala, *Science* **146**, 1073 (1964); M. C. Madsen and J. L. McGaugh, *J. Comp. Physiol. Psychol.* **54**, 522 (1961); A. Weissman, *ibid.* **56**, 806 (1963); D. Quartermain, R. M. Paolino, N. E. Miller, *Science* **149**, 1116 (1965).
2. J. L. McGaugh and L. Petrinovich, *Psychol. Rev.*, in press.
3. D. J. Lewis and H. E. Adams, *Science* **141**, 516 (1963); D. J. Lewis and B. A. Maher, *Psychol. Rev.* **72**, 225 (1965).
4. M. H. Friedman, *J. Comp. Physiol. Psychol.* **48**, 555 (1953); H. F. Hunt, *Trans. N.Y. Acad. Sci.* **27**, 923 (1965); C. P. Stone and A. H. Walker, *J. Comp. Physiol. Psychol.* **42**, 429 (1949).
5. W. B. Essman and H. Alpern, *Psychol. Rep.* **14**, 731 (1964).
6. Thirteen mice succumbed following the ether or shock treatments. The losses were distributed throughout the groups.
7. Previous research [for example, C. A. Pearlman, S. K. Sharpless, M. E. Jarvik, *J. Comp. Physiol. Psychol.* **54**, 109 (1961)] has shown that under some conditions ether anesthesia can produce retrograde amnesia. The anesthesia procedures of the present study would not, however, be expected to produce amnesia.
8. J. O. Ottoson, *Acta Psychiat. Neurol. Scand.* **35**, Suppl. 145, 103 (1960); A. Weissman, *Arch. Int. Pharmacodyn. Therap.* **154**, 122 (1965).
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Response during Sleep with Intervening Waking Amnesia

Abstract. *During stage 1 sleep, subjects responded to suggestions on two or more nights, up to 5 months apart. While they were awake they did not recall the material to which they successfully responded while asleep on a subsequent night.*

If a response has been established in the waking condition, subjects will respond during sleep to meaningful cognitive stimuli. Material presented during sleep alone, defined by electroencephalographic (EEG) criteria, is not recalled on awakening (*1*). However, some subjects respond while asleep to cue words associated with meaningful verbal suggestions that had been previously administered during sleep. Throughout administration of the suggestion and subsequent response to the cue, the subject remains in stage 1 sleep, defined by conservative EEG criteria (*2, 3*). Independently, Beh and Barratt (*4*) conditioned and extinguished EEG responses to mild shock in sedated sleeping subjects.

Objective response to meaningful material may be acquired during sleep and retained during periods of stage 1 sleep, but studies of sleep-learning imply that material presented during sleep is not retained after awakening. It is unlikely that the failure of retention after awakening is due to the time interval between sleep-acquisition and waking-recall. Delay between acquisition and response during sleep has been up to 5 hours, in several instances, without intervening awakening; a longer interval than that is frequently employed in sleep-learning studies (*3, 5*). Portnoff *et al.* (*6*) report that material presented during transient wakefulness is not learned unless it is followed by several minutes of wakefulness, which suggests that acquisition occurs only if consolidation occurs, or that any acquisition of responses during sleep cannot be accounted for by the occurrence of transient wakefulness during the acquisition process.

No attempt has been made in the sleep-learning studies to test whether acquisition had actually ever occurred. This could be done by testing retention during sleep. If acquisition and successful sleep-response are demonstrated during sleep, only then is it possible to investigate retention of the acquired response after awakening. Once these conditions are satisfied, waking retention may occur. If it does not, it is possible that material acquired during sleep remains relatively unavailable to waking-recall processes, in much the same way as dreams are often relatively unavailable to waking recall. This hypothesis may be tested by retesting the critical cue words during a subsequent sleep period.

Eighteen paid, male, student nurses each slept in a laboratory for two full nights. They were told only that *E* would be in the room occasionally.

Monopolar occipital, parietal, and frontal EEG were recorded with the use of standard procedures with an Offner Type-R 8-channel dynograph, which provided the sole basis for diagnosing ongoing stage 1 sleep according to criteria described by O'Connell *et al.* (*7*). Suggestions were repeated twice by *E* in a low monotone, and no attempt was made to determine whether *E*'s words were presented above sleeping auditory thresholds. No suggestion or cue word was spoken if the technician signaled the presence of visually detectable alpha-frequency activity superimposed on the otherwise flat, desynchronous, emergent stage 1 EEG record. Although rapid eye movements (REM), inferentially associated with dream reports, occur during this stage of sleep, the presence or absence of REM activity was not considered in the diagnosis of ongoing stage 1 sleep. Stage 1 (descending) sleep following awakening was not used.

The suggestions required a clearly identifiable overt response, and a subjectively experienced (usually negative) affect. A typical suggestion was, "Whenever I say the word 'leg,' your left leg will feel extremely cramped and uncomfortable until you move it." The suggestion was tested by repeating once the cue word "leg." Subsequent repetitions of the cue word were not made for at least 60 seconds. A response was considered successful only if the suggested specific movement was made.

The first suggestion was administered during the first emergent stage 1 period and was then tested. During the next stage 1 period, the same suggestion was tested again, and a new suggestion was administered. Both suggestions were tested, with the appropriate cue word alone, during all subsequent periods of stage 1 sleep that night. Frequency of testing the suggestions varied, depending partly on the subject's level of arousal during the night.