Recovery from Retrograde Amnesia: A Learning Process

Abstract. *Retrograde amnesia was produced in rats by electroconvulsive shock. Memory recovered if the animals were given repeated test trials. Memory did not recover if steps were taken to reduce the conditioning properties of the test trials; the manipulations included eliminating the response, altering the apparatus cues, or extinguishing conditioned "fear" by confining animals to the apparatus during the first test trial.*

It is commonly held that the neural code for memory storage changes with age: short-term memory is thought to be stored in a vulnerable state, long-term, established memory in a resistant state, and the process that mediates the transformation from one state to the other is referred to as memory consolidation (*1*). Support for this position comes largely from data indicating that neural trauma disrupts short- but not long-term memory. In rats, for example, electroconvulsive shock (ECS) delivered 0.5 second after training produces amnesia; ECS delivered 30 seconds after training has no effect on retention (*2*). Consistent with a memory consolidation interpretation, the data are taken to indicate that the 0.5-second-old memory is in a vulnerable state and the 30-second-old memory is in a resistant state.

The notion of memory consolidation has been challenged by a simple but perplexing observation. One would expect that if ECS destroyed short-term memory and thereby prevented consolidation, then its amnesic effects should be permanent. Amnesia following ECS, however, is often not permanent. Recently, Quartermain, McEwen, and Azmitia (*3*) defined some of the boundary conditions necessary to restore retention following ECS-induced amnesia. During training, rats were given a single punishing footshock for stepping from a small to a large compartment and were convulsed 1 second later. During testing, the rats were given one trial per day for the next 3 days. For the first 2 days, the rats showed little or no sign of retaining the avoidance and tended to step from the small to the large compartment. On the third day, the rats showed recovery of retention and tended to avoid stepping through. Further analysis suggests that the test-trial procedure itself is critical in restoring retention; animals not given test trials, but simply left in their home cages for several days, show no recovery when finally tested (*4*).

In this report we advance a new theory and present supportive data to account for the selective-amnesic effects of ECS on short-term memory and the recovery properties of test trials. The crux of the theory is the assumption that during passive-avoidance training, when the animal steps from the small to the large compartment and is punished, two associations are formed: one association is made between the response and punishment (commonly referred to as instrumental conditioning) and the other is made between the cues in the large compartment and punishment (commonly referred to as classical conditioning). Furthermore, it is assumed that ECS, when delivered immediately after training, affects the two associations differently; ECS disrupts short-term storage of the instrumental association but does not affect storage of the classical association. Finally, it is assumed that the survival of the classical association following ECS is not sufficient for the retention of the avoidance response, at least initially, but is necessary in promoting later recovery during repeated test trials. Specifically, during the initial test trials when the amnesic animal quickly steps from the small to the large compartment, it comes into contact with and is punished by the classically conditioned aversive stimuli which presumably survive the disruptive effects of ECS. The conditioned stimuli in turn work in the same way as, but perhaps to a lesser extent than, the footshock during training to recondition the instrumental association. In summary, according to the theory, retention of the avoidance response depends on the integrity of the instrumental association, ECS destroys short-term storage of the association, and the repeated test trials, because of their enduring classically conditioned aversive properties, serve as learning trials for reconditioning the instrumental association. To test the theory we first confirmed that the test trials are essential for recovery, and then extended the analysis to show that they promote recovery by serving as learning trials.

The subjects were 70 male albino rats of the Sprague-Dawley strain, weighing 225 to 275 g. The training apparatus was a standard passive-avoidance two-compartment box (*5*). The first day consisted of a habituation trial in which the animals stepped from a small lit to a large dark compartment, but did not receive punishing foot-

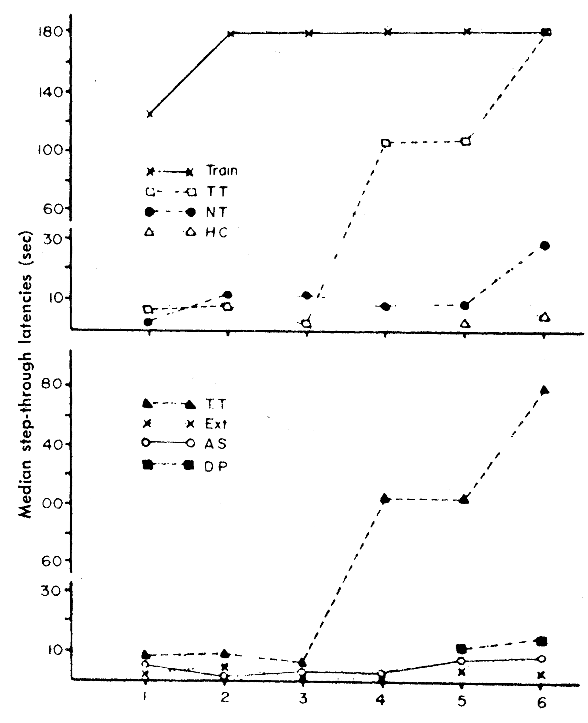

Fig. 1. Median step-through latencies for the retention-test trials. The upper panel depicts the effects of repeated test trials (*T.T.*) and home cage (*H.C.*) on recovery. The lower panel depicts the effects of direct placement (*D.P.*), altered stimulus conditions (*A.S.*), and extinction (*Ext.*) on recovery. Each group contains ten subjects. The recovery curve for the *T.T.* group is duplicated in both panels. *Train*, trained controls; *N.T.*, nontrained controls.

shock. On the second day, each animal received conventional passive-avoidance training in which they were punished with footshock (1.6 ma, 2 seconds) for stepping from the small lit to the large dark compartment; ECS (35 to 50 ma, 0.3 second) was delivered through ear snaps 1 second after training. Following ECS the animals were divided among five groups and were given different test procedures for the next 6 days. Two control groups, one given training but no ECS and the other given ECS but no training, received conventional testing (*6*), one trial per day, for the next 6 days.

The retention data are presented in Fig. 1; as step-through latencies increase, retention is taken to increase (*7*). In the groups given ECS, a significant reduction in step-through latencies relative to the trained controls (*Train*) is taken to reflect amnesia, and a significant increase in step-through latencies relative to the nontrained controls (*N.T.*) is taken to reflect recovery.

It can be seen from Fig. 1 (top panel) that we replicated the basic retrograde amnesic and recovery effects. Group *T.T.* (test trials), given conventional testing, one trial per day, showed amnesia until day 4, when retention finally recovered to the level of the trained controls. We also reaffirmed the importance of the test trials for recovery. Group *H.C.* (home cage), given no test trials but rather returned to their home cage for 4 days and then tested on days 5 and 6, showed no signs of recovery.

Data presented in Fig. 1 (lower panel) comparing the remaining three ECS-treated groups with the conventional recovery group (*T.T.*) provide support for the learning interpretation of recovery. Each group received a different manipulation calculated to weaken the instrumental conditioning properties of the test trials and in each case recovery was suppressed. For some animals (*D.P.*, direct placement) we eliminated the step-through response during testing. The animals were placed directly in the large dark compartment during the first four test trials, a 5-second exposure per trial, and then were given conventional test trials on days 5 and 6. For other animals we used two different procedures in an attempt to weaken the conditioned-aversive properties of the apparatus during testing. In one case (*A.S.*, altered stimulus) we changed the stimulus conditions from training to testing. During testing the animals stepped from the small to the large compartment. The small compartment was lit as usual, but the large compartment, which was dark during training, was now also lit. In the other case (*Ext.*, extinction), in an attempt to extinguish the aversive properties of the apparatus, we gave the animals prolonged exposure to the apparatus during the first test trial. Specifically, the animals, as usual, stepped from the small to the large compartment, but once in the large compartment they were confined for 8 minutes before being removed (*8*). On the next 5 days the animals received conventional test trials.

The results are clear: animals recover from retrograde amnesia as long as we preserve during testing both the step-through response and the conditioned-aversive properties of the apparatus (*9*). The implications are also clear: (i) test trials induce recovery by promoting learning and (ii) ECS disrupts storage of instrumental but not classical conditioning. Here, however, caution must be exercised. We do not mean to imply that storage of the classical association is indestructible. In fact, classical storage may be just as vulnerable as instrumental storage, but, unlike instrumental storage, may involve neural circuits outside the influence of ECS (at least 35 to 50 ma, 0.3 second). Indeed, others have found that removal of cortex in rats prevents instrumental but not classical conditioning, affirming at least a cortical distinction between the two associations (*10*).

Finally, although our conclusion regarding the differential sensitivity of the two types of conditioning to ECS is based on inferences from the recovery data, it should be emphasized that these data do not stand alone in support of the notion. Recently it has been reported that ECS delivered immediately after passive-avoidance training disrupts retention of skeletal (that is, step-through response) but not visceral (that is, heart-rate suppression) responses (*11*). Given that retention for each type of response calls for a different type of conditioning, skeletal calling for instrumental and visceral for classical conditioning, then these data, too, may be taken as evidence for the notion that classical associations lie outside the influence of ECS.

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References and Notes

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6. Conventional testing consisted of allowing animals to step from the small to the large compartment, not delivering footshock, and removing them 5 seconds later. If an animal remained in the small compartment for 180 seconds, the test trial was terminated.
7. A Mann-Whitney U test (two-tailed) was used for statistical evaluation. For each statistically significant result the *P* value was less than .05.
8. Control animals confined to the small lit rather than the large dark compartment during the first test day showed normal recovery, thereby ruling out the possibility that confinement per se is sufficient to prevent recovery.
9. We have also found that recovery can be obtained within four test trials by (i) reinstating normal stimulus conditions (that is, those stimuli operating during training) after the animals show no recovery with altered stimulus conditions and (ii) confining the trials, using a 1-minute intertrial interval, to the first test day.
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North Carolina Glacier: Evidence Disputed

A field check of the grooves reported by Berkland and Raymond (*1*) indicates that they are man-made rather than glacial. Characteristics observed include the following: (i) a relatively narrow range in width, 1.5 to 2.0 cm [figure 2 in (*1*) shows not one 15-cm-wide groove but rather a single groove to the left of a triple groove]; (ii) the presence of a ferric stain in the bottom of some grooves; (iii) polish on groove bottoms but not on intergroove surfaces; (iv) the presence of at least one groove that continues partially down the vertical face of the outcrop; and (v) the absence of grooves in shallow lows of the outcrop surface [figure 3 in (*1*)]. These points plus the discovery of weathered wire cable of two diameters —1.1 and 2.0 cm—0.5 km downslope imply that the grooves are a product of building stone quarrying (*2*), log-