Effect of ACTH on ECS-produced amnesia of a passive avoidance task*

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Rats given electroconvulsive shock following a one-trial passive avoidance step-down task showed amnesia for that task. Administering adrenocorticotrophic hormone, 4 h after training, produced recovery of the avoidance behavior. This suggests that reactivating the internal physiological state present during training is sufficient to retrieve memories that are inaccessible following electroconvulsive shock.

Hebb (1949) has suggested that following sensory input, a neural consolidation process, operating over time, permanently fixes the memory trace. Electroconvulsive shock (ECS) produces massive electrical interference, which, if given during the consolidation period, should disrupt the neural activity and thereby prevent the permanent fixation of memory (McGaugh & Herz, 1972). Administering ECS shortly after a one-trial learning experience, then, should result in permanent retrograde amnesia (RA) for that experience (Lewis, 1969).

Recently, the permanence of this RA has been questioned (Miller & Springer, 1973; Spear, 1973). Lewis, Misanin, and Miller (1968) have shown that with a one-trial passive avoidance task followed by ECS, administering a "reminder" footshock at a later time, eliminates the RA. Miller and Springer (1972) found that the RA could be eliminated with ECS-reminder intervals as long as 336 h.

Other experiments have shown that reactivating a consolidated memory and following this reactivation with ECS produces apparent amnesia (Misanin, Miller, & Lewis, 1968; DeVietti & Holliday, 1972). The time between training and reactivation was 24 h in these studies, an interval that insures consolidation. These combined studies suggest that ECS may not affect memory storage, but rather may interfere with retrieval mechanisms.

Springer and Miller (1972) have shown that, in avoidance learning, the aversive training stimulus and the reminder agent do not have similar physical properties. They used ice-water immersion as the training stimulus and footshock as the recovery agent. Footshock was an ineffective recovery agent, however, when an appetitive task was used (Miller & Springer, 1973). This indicates that footshock does not serve as a universal recovery agent.

Klein (1972) has shown that the retention deficit found after an intermediate retention interval with the Kamin effect can be eliminated by administering adrenocorticotrophic hormone (ACTH). Klein suggests that ACTH may mediate aversive memories. Levine and

Brush (1967) suggest that ACTH administration reinstates the motivational cues associated with avoidance training. Howard, Glendenning, and Meyer (in press) found that long-term habits could be disrupted by ECS if ECS was given when the organism learned another task that was based on the same motivation.

From this data, it seems that retrieval agents may be effective because they reintroduce the internal physiological state (motivation) present during training. The present experiment was conducted to determine whether or not ACTH could produce memory retrieval.

METHOD

Subjects

The Ss were 96 naive male albino rats, 200-250 g in weight at the start of the experiment.

Apparatus

The apparatus consisted of a chamber enclosed in a sound-insulated ventilated cubicle. The chamber had a grid floor and a step-down platform, 2.0 cm high, in one of the corners.

A separate box made of Plexiglas was used to administer the reminder footshock.

Procedure

The Ss were selected randomly from the LSU colony and placed in individual cages. The Ss were given ad lib food (Purina Chow) and water throughout the experiment.

For 5 days, Ss were handled in pairs for 5 min per day. On the next day, S was placed on the platform and a timer was started. When S stepped off the platform (both forepaws), the timer was stopped and S received one of the following treatments: a 2-sec 3-mA footshock, delivered through the grid floor, followed immediately by a 50-mA 500-msec ECS delivered through earclip electrodes (SECS), a 2-sec 3-mA footshock (SO), a 50-mA 500-msec ECS (ECS), or no treatment (OO). These treatments were termed the original treatments.

Four hours after the original treatments, Ss received one of the following retrieval treatments: footshock (FS), consisting of a 2-sec 3-mA shock delivered in the Plexiglas box, an interperitoneal (IP) injection of 10 units of ACTH (ACTH)pH = 7.4 or an IP injection of physiological saline (NT). The E wore a white laboratory coat and gloves when administering the reminder treatments in order to minimize cues associated with training.

Three-millamp footshocks and ACTH injections of 10 units were used because they seem to have comparable effects. Sayers and Travis (1970) have shown that ACTH is released by painful stimulation such as electric shock. Bush (1962) suggests that circulating corticosteroid levels are largely or entirely under the

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Table 1
Mean Step-Down Log Latencies on Test Trial

Group	Latency	Group	Latency
SECS-ACTH	1.565	ECS-ACTH	0.714
SECS-FS	1.536	ECS-FS	0.565
SECS-NT	0.591	ECS-NT	0.627
SO-ACTH	1.575	OO-ACTH	0.620
SO-FS	1.542	OO-FS	0.682
SO-NT	1.550	OO-NT	0.650

control of ACTH. Levine and Brush (1967) have shown that an ACTH injection of 10 units significantly elevates plasma corticosterone levels. Friedman et al (1967) found that a footshock, 2-4 mA, produces a comparable elevation in corticosterone levels.

Retention testing was conducted 24 h after retrieval treatment administration. The S was placed on the platform, and the timer was started. When S stepped off the platform (both forepaws), the timer was stopped and the latency recorded. Retention trials were terminated if S stayed on the platform for 120 sec.

RESULTS

There were no differences among the groups in the step-down latencies on the training trial (Mann-Whitney U). Therefore, the retention trials were analyzed directly.

The retention trial latencies were converted to log latencies in order to permit parametric statistical analysis. These data were subjected to an analysis of variance, which showed that the original treatment and the retrieval treatment main effects were significant beyond the .01 level. The Original Treatment by Retrieval Treatment interaction was significant beyond the .01 level also. A priori group comparisons (t tests) were conducted. In the group abbreviations, the first abbreviation refers to S's original treatment following the training trial and the second abbreviation refers to the reminder treatment administered 4 h later. The a priori group comparisons showed that the comparisons OO-NT vs OO-FS, OO-NT vs OO-ACTH, SECS-FS vs SECS-ACTH, OO-NT vs ECS-NT, OO-NT vs ECS-FS, OO-NT vs ECS-ACTH, SO-NT vs SECS-FS, and SO-NT vs SECS-ACTH were not significant at the .05 level. The comparisons SO-NT vs OO-NT, QSCS-NT vs SO-NT, SECS-NT vs SECS-FS, and SECS-NT vs SECS-ACTH were significant beyond the .01 level. The mean step-down log latencies for all groups is shown in Table 1.

DISCUSSION

The finding that Ss receiving footshock upon stepping off the platform had significantly longer latencies on the retention trial than Ss given no treatment indicates that this was an effective one-trial passive avoidance task. Rats given footshock followed by ECS showed apparent RA for the footshock. This result is in agreement with other findings (Lewis, 1969; McGaugh & Herz, 1972).

The finding that noncontingent footshock given after training serves as an effective retrieval agent is also in agreement with other studies (Lewis, Misanin, & Miller, 1968; Miller & Springer, 1972).

A critical finding of this study is that ACTH is also an effective retrieval agent, producing recovery from ECS-produced amnesia. Ss given only the footshock or the ACTH reminder treatment were not significantly different from the no-treatment Ss. This suggests that any change seen after retrieval treatment cannot be attributed to a direct effect of noncontingent footshock or ACTH on step-down performance. The results further show that footshock and ACTH both produce relatively complete recovery from ECS-induced amnesia.

The combined findings suggest that the retrieval agents are effective not because they have physical properties similar to the training stimulus, but rather because they reinstate an internal physiological state, motivation, that is similar to that present during training. Similarly, Levine and Brush (1967) suggest that the elimination of the retention deficit seen at intermediate retention intervals with the Kamin effect following ACTH administration is because ACTH reinstates the motivational cues' associated with avoidance training.

Miller and Springer (1973) report that footshock is an ineffective retrieval agent when an appetitive task is used. This suggests that simple arousal cannot account for the retrieval phenomenon since footshock produces arousal. Rather, in the light of the present findings, footshock would seem to be ineffective in this situation because its internal consequences are not similar to the internal state present during training.

The combined findings suggest that ECS disrupts retrieval mechanisms and not storage mechanisms. Information is stored by the organism, but is inaccessible. Reinstating an internal physiological state similar to that present during storage allows the organism access to these memories or engrams. The retrieval phenomenon mechanisms, therefore, seem to be motivational in nature.

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