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BRIEF COMMUNICATION

The Effect of Scopolamine on the Amnesia Induced by Electroconvulsive Shock[1]

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ALBERT, D. J., C. J. MAH AND W. B. BOSE. *The effect of scopolamine on the amnesia induced by electroconvulsive shock.* PHARMAC. BIOCHEM. BEHAV. 2(3) 443–446, 1974. – Rats previously allowed to drink water from a spout received a mouth-shock at the spout as one-trial avoidance training. In animals where a pair of ECSs followed the mouth-shock, a retention test 48 hr later revealed a reliable amnesia relative to sham ECS animals. When scopolamine was injected 30 min prior to the test trials, the amnesia was unchanged. The present results do not confirm previous suggestions that scopolamine can completely reverse ECS-induced amnesia.

Amnesia Cholinergic Electroconvulsive shock Memory Scopolamine

WHILE electroconvulsive shock (ECS) impairs retention when administered shortly following learning, it also produces a disturbance of brain acetylcholine levels [2,16]. Accordingly the impairment of retention caused by ECS may be due to the alteration of brain acetylcholine. In support of this possibility, Adams, Holbit, and Sutker [2] and Davis, Thomas and Adams [6] have found attenuation of ECS-induced amnesia for active and passive avoidance by the anticholinergic drug, scopolamine. However, the applicability of these results to other experiments in the ECS literature is questionable because of the short delay (4 hr) between ECS and testing. In contrast, most studies on ECS-induced amnesia allow a longer interval (24–48 hr) for recovery from ECS.

The intent of the present experiment was to determine whether the anticholinergic drug scopolamine could reverse ECS-induced amnesia of passive avoidance learning. Amnesia was induced by two ECSs given 1 min apart, since there is some evidence that this is more effective than a single ECS for producing amnesia [13]. To allow for adequate recovery from the aftereffects of ECS, the animals were not tested for retention until 48 hr following training.

METHOD

Animals

The animals were 82 experimentally naive, male hooded rats (235–270 g) from the Canadian Breeding Farms and Laboratories. They were housed in individual cages throughout the experiment.

Surgery

Electrodes for administering ECS were implanted bilaterally over the dorsolateral cortex. The electrodes consisted of a pin soldered onto the end of a stainless-steel screw (1 mm dia.).

Apparatus

The passive avoidance apparatus was a box 40 x 40 cm square and 40 cm deep. The inside was painted flat black and there was a grid floor. Midway along one wall and 2 cm above the floor was a 6 x 6 cm opening to a nook (9 cm deep). Bored into the top of the nook, 4 cm from the edge was a hole (8 mm dia.) which was just large enough for a drinking spout. When in place, the spout projected 3 cm down into the nook (see Albert and Mah [3,4] for a more thorough description of the apparatus).

Latency to drink was recorded by means of an automatic timer connected to a drinkometer. The length of the training session in the apparatus was controlled by a preset timer which also started the latency timer.

During the passive avoidance training, shocks were delivered to the animal when it completed a circuit from the

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spout to the grid. The shock was generated by a 460 V transformer in series with 85,000 ohm resistance. Latency to receive shock was timed with an automatic timer.

Electroconvulsive shock was generated through a 60 Hz, 820 V transformer connected in series with a 15,000 ohm resistor. The effective current was about 55 mA and the duration was 0.45 sec.

Experimental Design

Three variables were manipulated: ECS, mouth shock, and drug injection. To examine all combinations of variables a 2 × 2 × 2 factorial design was used (Fig. 1). This required 8 groups of animals. All were treated the same during preliminary approach training and were separated randomly into groups at the beginning of avoidance training. Then as required by the factorial design, half of the animals received mouth shock (MS) and the others received no mouth shock (NMS); half of the animals received ECS following the training trial and the other animals were given a sham ECS (NECS); and then prior to testing, half of the animals were injected with scopolamine (Scop) and the others were injected with 0.9% saline (Saline).

In addition to these 8 groups, one other group was included to show that the effect of the ECS on retention of the passive avoidance learning is time dependent. This group received a mouth shock, then an ECS 6 hr later. Following passive avoidance training water was given to this group at the same time as it was to the others. Prior to retest, this group received a saline injection.

Training and Testing Procedure

The animals were water-deprived 24 hr before surgery and were then maintained on a 23 hr water deprivation schedule for the remainder of the experiment. On each day water was given for 1 hr at about the time it would be given during the training and testing period.

Approach training began 5 days following surgery (Day 1). The animal was taken from its cage and placed in a carrying box beside the apparatus for 1 min. Each animal was grasped by the tail and placed into the apparatus facing away from the nook. The animal remained in the apparatus for 5 min. Latency to drink was recorded automatically. On the next day (Day 2), the animals were also given 5 min in the apparatus and the latency to drink recorded.

Avoidance training was given on Day 3. After the animal had made 5 licks at the spout, a relay automatically disconnected the drinkometer and connected the shock current between the spout and the grid. The animal was removed from the apparatus 15 sec after the mouth-shock. For animals whose treatment condition did not involve shock, removal from the apparatus occurred 15 sec after making 5 licks.

Following the avoidance trial, all animals received either ECS or sham ECS. The sham ECS consisted of connecting clips to the electrodes for 15 sec and then returning the animals to its home cage. The animals receiving ECS were treated in the same way except that a 55 mA current was passed through the electrodes for 0.45 sec as soon as the electrode clips were attached. One min later a second ECS current was passed through the electrodes. The first current elicited a full tonic-clonic convulsion and the second a clonic convulsion. The delay between mouth shock and ECS was 30 sec. The animals were returned to their cage

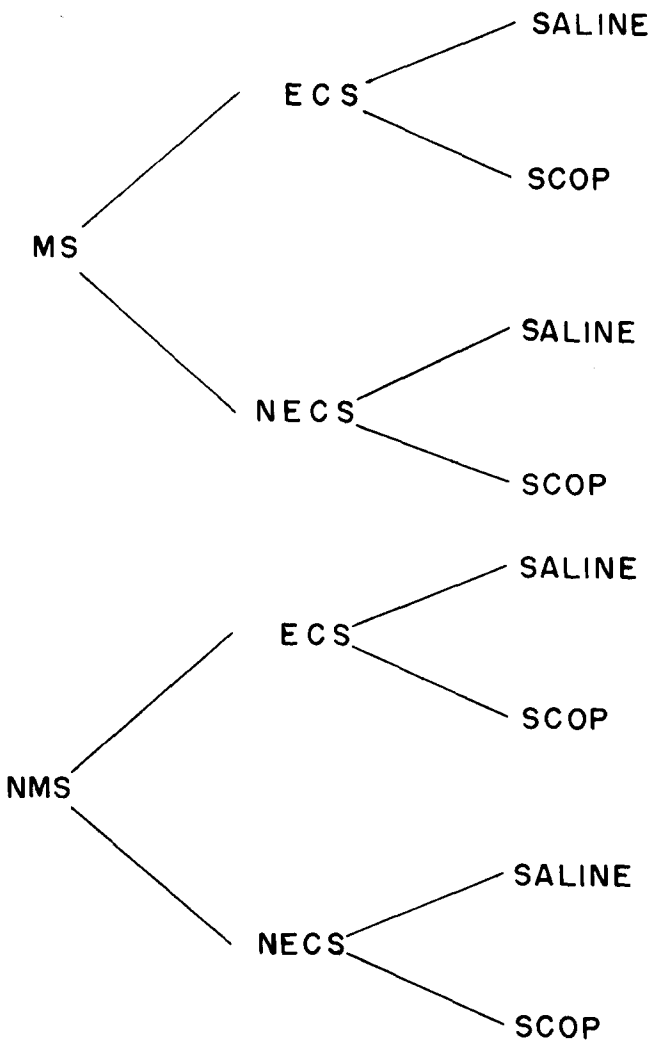

FIG. 1. The design of this experiment.

while convulsing. Water was given for 1 hour beginning 1-1/2 hrs following the training of the last animal.

On the day following avoidance training (Day 4) no training or treatment of any kind was given. The animals had access to water in their home cage for 1 hr at about the same time as it was usually given.

A retention test was given to each animal on Day 5. Thirty min before being tested each animal was given an injection of 0.9% NaCl (0.05 ml) or hyosine hydrobromide (1 mg/kg, Scopolamine, Glax-Allenburys, Canada). Testing was then carried out in the same way as approach training on Day 2; the animals were left in the apparatus for 5 min and the latency to drink was automatically recorded.

Statistical Analysis

Response latencies were subjected to a one-way analysis of variance by ranks (Kruskal-Wallis) to confirm that overall differences between groups existed. Individual paired comparisons were then made with the Mann-Whitney U Test.

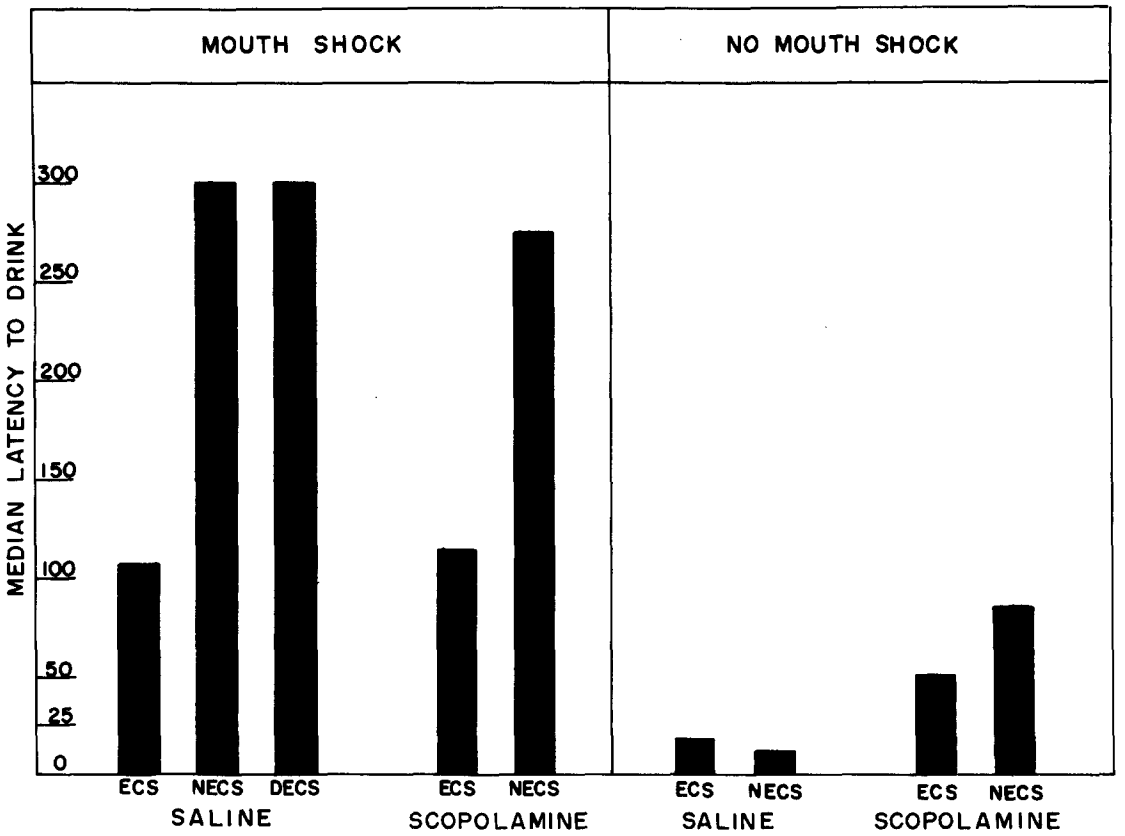

FIG. 2. The effect of mouth-shock, ECS and scopolamine on latency to drink at testing. The groups on the left first received mouth-shock to create avoidance of the spout and then ECS or sham ECS. The groups on the right received an ECS or sham ECS without the avoidance-producing mouth-shock. Scopolamine or saline injections were given 30 min before the test sessions.

RESULTS

Retention of the passive avoidance of the spout (Fig. 2) was impaired by administration of 2 ECSs following the punishing mouth shock. The median latency to drink for the group receiving a mouth shock and a sham ECS (MS-NECS-Saline; N = 8) was 300 sec. For the group where mouth shock was followed by ECS (MS-ECS-Saline; N = 9), the latency to drink was significantly lower (median = 108 sec, U = 7, $p<0.02$). When the ECS was delayed for 6 hours following mouth shock (MS-DECS-Saline; N= 10) the latency to drink was 300 sec, not different from the latency of the group receiving mouth shock alone.

These results establish that the punishing mouth shock used in these experiments does produce good passive avoidance of the spout on the test day and that this avoidance tendency is greatly attenuated by an ECS which is given shortly but not 6 hr following the mouth shock.

Scopolamine injected one-half hour before training did not alter either the passive avoidance behaviour or the attenuation of that behaviour by ECS. The animals which received mouth shock, a sham ECS, and then scopolamine prior to testing (MS-NECS-Scop; N = 8) showed a strong passive avoidance tendency (median 273 sec) whereas the group receiving a mouth shock, ECS and then scopolamine before testing (MS-ECS-Scop; N = 11) avoided significantly less (median 114 sec, U = 16, $p<0.05$). Inspection of Fig. 2 reveals that the median response latencies of the groups receiving mouth shock and injected with scopolamine are almost identical to those of their respective matched groups which were treated in the same way except that they were injected with saline.

Figure 2 also shows the effect of scopolamine and ECS on the approach response. With saline alone (NMS-NECS-Saline; N = 8) median latency to drink was 12 sec. This was not significantly changed by 2 ECSs administered 48 hr earlier (NMS-ECS-Saline; N = 10; latency 18 sec). With scopolamine alone (NMS-NECS-Scop; N = 9) median latency to drink was 84 sec. When ECS was given 48 hr before testing (NMS-ECS-Scop; N = 10) the latency to drink was 51 sec not reliably different from that of animals not given ECS.

DISCUSSION

The latency to drink of the MS-ECS groups are highly similar regardless of whether saline or scopolamine was injected prior to the retention test. From this it is clear that we did not obtain the strong reversal of amnesia reported by Adams *et al.* [2] and Davis *et al.* [6]. It seems unlikely that the failure to obtain a reversal of the amnesia is attributable to a dose effect since our dosage was the same as that used in both the Adams and Davis studies. Presumably,

therefore, the difference in results is due to procedural differences. The most important of these is that Adams *et al.* [2] and Davis *et al.* [6] used a 4 hr ECS-test interval while we used a 48 hr ECS-test interval.

The present findings are interpretable within a consolidation framework. The mouth shock produced a strong avoidance of the water spout. This avoidance tendency was substantially reduced in animals receiving ECS, indicating there was an amnesia for the mouth shock. The amnesia was not reduced by administering scopolamine 30 min prior to testing. Thus, it would appear that in the present experiment, the amnesia for the passive avoidance learning is not dependent on an elevation of acetylcholine level at the time of testing which can be reduced by scopolamine. Consistent with the present evidence that brain acetylcholine changes cannot fully account for the amnesia produced by ECS are a number of experiments reporting little or no recovery from ECS-induced amnesia during the time period when the altered acetylcholine levels are reverting to normal through biological processes [5, 7, 8, 10, 15].

There remains the question as to why the ECS-induced amnesia obtained by Adams *et al.* [2] and Davis *et al.* [6] was reversed by scopolamine when testing was at 4 hr following ECS. A number of experiments [9, 11, 14] including one by Adams and Calhoun [1] have found spontaneous recovery from ECS-induced amnesia. The reasons why the amnesia is temporary in these cases is only partly understood [12]. However, the scopolamine-induced reversal of amnesia obtained by Adams and coworkers [2,6] may be the result of having an amnesia that would have reversed over time spontaneously. The normalization of brain cholinergic systems may be one factor that is involved in this spontaneous recovery.

A final point concerns the interaction of scopolamine and ECS on drinking when mouth shock is not given (Fig. 2). At 48 hr following ECS there is no effect of scopolamine on latency to drink relative to saline. However, when ECS is not given, scopolamine does cause a significant increase in drinking latency ($p<0.05$).

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