hypothesis that the septal area modulates the effects of light stimulation, and that in the absence of such modulation, because of the lesion, light stimulation becomes highly aversive for septal animals. This remains for further investigation.

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NOTES

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Physostigmine: Effects on retention at different times after brief training

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Mice were given physostigmine 30 min, 1 day, 3 days, 7 days, or 14 days after brief training in a position habit, which normal animals forget within 14 days. The curve generated by the retention scores at these times was a miniaturization of the curve generated by previous studies using anticholinesterases and prolonged training in a visual task.

Cholinesterase inhibition is known to affect performance depending on when after training it is initiated (Deutsch, 1969; Squire, 1969). Three different effects on the retention of a well-learned visual discrimination have consistently been obtained following the administration of anticholinesterases at different times after training (Deutsch, Hamburg, & Dahl, 1966; Deutsch & Leibowitz, 1966). Early in the lifetime of the habit (1-3 days), retention is normal. Subsequently (7-14 days), anticholinesterase impairs retention. Finally, late in the lifetime of the habit, when forgetting can be observed (28 days), retention is improved. If these effects reflect, as has been postulated, specific, sequential changes in memory fixation, then habits of shorter lifetimes might reveal the same sequence of effects, though not necessarily at the same time after training.

SUBJECTS AND APPARATUS

The Ss were 271 male albino mice

obtained from Charles River Breeding and weighing 35-40 g at the time of training. They were housed 10 to the cage and provided with ad lib access to food and water. The apparatus was a T-maze with stem 12 in. long and each arm 7 in. long. The walls were 11½ in. high. The floor was a grid of 5/32-in. stainless steel rods, spaced ½ in. apart, that could be charged with scrambled .4-mA current.

PROCEDURE

For training, a mouse was placed on the charged grid of the T-maze facing the choice point. If it ran to the correct side, the shock was terminated and, 5 sec later, was removed from the maze and placed on a table. If the mouse ran to the incorrect side, the shock remained on until it entered the correct arm. Training continued with an intertrial interval of 15-25 sec until a mouse made three correct choices in four consecutive trials. Half of the mice were trained to choose the left arm of the maze and half were trained to choose the right arm. The procedure during retention tests was identical to that during original training. Retention testing continued until a mouse attained a criterion of three correct choices in four consecutive trials.

Mice were assigned to one of five groups, which were tested for retention 45 min, 1 day, 3 days, 7 days, or 14 days after completion of original training. Half the mice of each group were given physostigmine salicylate (.4 mg/kg) I.P. 15 min before the retention test. The other

half were given an equivalent volume of distilled water vehicle. Those mice failing during original learning to reach criterion within 12 trials (N = 6) were eliminated. Thirteen mice given physostigmine did not consistently run in response to shock during the retention test and were discarded. Those mice requiring more than 12 trials to reach criterion during retention (N = 7) were assigned a retention score of 12.

The difference scores (trials to learn - trials to relearn) for each group closely approximated a normal distribution. Accordingly, two-tailed t tests were used to compare the difference scores of independent groups. Savings within groups were evaluated with Wilcoxon matched-pairs, signed-ranks tests.

RESULTS

The mean number of trials required to reach criterion during original learning was 5.1 (range of means for 10 subgroups, 4.9-5.6). Trials to criterion during retention tests for both experimental and control groups are presented in Fig. 1. Control animals exhibited savings when tested 45 min, 1 day, 3 days, or 7 days after learning ($p < .05$), but forgot the task within 14 days. After 14 days, control animals required as many trials (5.5) to relearn the task as had been required to learn it originally. Mice given physostigmine and tested 45 min, 1 day, or 3 days after training exhibited significant savings at each interval ($p < .05$), and were not significantly different from control Ss given their retention tests at the corresponding times. However, mice given physostigmine 7 days after training did not exhibit savings. They learned originally in 5.2 trials and, 7 days after training, required 4.7 trials to relearn ($p > .1$). The difference between the scores of experimental and control mice did not reach significance ($t = 1.1, p > .2$). Finally,

Fig. 1. Trials required to relearn the task at different times after training. The numbers in parentheses indicate the number of mice in each group. O indicates the mean number of trials required by all mice to learn the task originally.

14 days after training, at a time when control mice had completely forgotten the position task, mice given physostigmine exhibited significant retention ($p < .01$). Their performance during retention was significantly better than that of control mice tested 14 days after training ($t = 2.1$, $p < .05$). Furthermore, control mice performed significantly better 7 days than they did 14 days after training ($t = 2.1$, $p < .05$). Mice given physostigmine before testing performed significantly worse 7 days than they did 14 days after training ($t = 3.2$, $p < .01$).

DISCUSSION

The results indicate that an anticholinesterase agent affects performance depending on when it is given. The shape of the retention curve for mice given physostigmine closely resembles the curve for rats given the anticholinesterase DFP after prolonged training on a visual discrimination motivated by shock (Deutsch, Hamburg, & Dahl, 1966; Deutsch & Leibowitz, 1966) or by thirst (Wiener & Deutsch, 1968), and also resembles the curve for rats given physostigmine after prolonged training on a visual discrimination motivated by shock (Hamburg, 1967). The fact that physostigmine, like DFP, can improve performance at the time when normal animals forget has not been previously demonstrated. The longest retention interval used in the study by Hamburg (1967) was 14 days, and at this interval normal animals remembered a visual discrimination quite well.

In the present study, mice given physostigmine 30 min after training were not significantly impaired in retention. A slight, but significant, impairment has been reported at this time interval (Deutsch et al, 1966; Hamburg, 1967), but it has not

always been observed (Wiener & Deutsch, 1968).

The lifetime of the well learned visual habit is about 28 days. The lifetime of the undertrained spatial habit is only 14 days. Improved retention produced by anticholinesterase appeared as a reversal of normal forgetting in both cases and did not depend on the passage of a fixed amount of time after training. In the visual task, the impairment at 7-14 days represented almost total amnesia. In the spatial task, only partial amnesia was observed at 7 days. This difference might depend on differences in species or on differences between visual and spatial tasks. It might also depend specifically on the difference in lifetimes of the two habits or on the difference in strength of original learning. Deutsch & Lutsky (1967) have demonstrated that amnesia produced by DFP is greater for a well learned habit than for a poorly learned habit. Accordingly, it is possible that the acquisition of rapidly forgotten habits, like more permanent habits, initiates gradual physiological changes that continue for several days. The rate of these changes or their final extent may be less in habits that are soon forgotten than in habits that are not so readily forgotten.

It is thus conceivable that this gradually changing process might be understood in terms of a gradual increase in transmission at central cholinergic synapses, as has been suggested (Wiener & Deutsch, 1968), but this proposal remains tentative, at least until the possibility of a role for peripheral cholinergic systems in these phenomena is evaluated. Tests of this possibility are in progress in this laboratory. Whatever the specific interpretation, these results are consistent with the suggestion that aspects of the memory process continue to change for days or perhaps weeks after training

(Flexner, Flexner, & Stellar, 1963; Rosenbaum, Cohen, & Barondes, 1967; Squire & Barondes, 1970).

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