EFFECTS OF SOME TRANQUILLIZERS ON LEARNING AND MEMORY TRACES IN RATS *

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Effects of some psychoactive drugs on acquisition and memory traces have been reported by several workers (1,7,9). These investigators employed conditioning techniques in their studies. Buresova et al. (3) and Jarvick and Byck (5) have studied the effects of atropine and physostigmine, and ether and electroconvulsive shock respectively on learning and memory traces in rats and mice using single but two different types of one-trial learning technique. One trial learning procedure (3,5) being simple and also gives the precise age of memory traces, which is not possible with conditioning techniques where animals are exposed to many trials. In this paper, however, we have used the simple one-trial learning procedure of Buresova et al., (3) to study the effects of some tranquilizers—chlorpromazine and reserpine—on learning, retrieval (recollection of passive avoidance reaction), consolidation phase of memory traces and permanent memory in rats. Effects of 1-(β-phenylethyl) triazolo (4,5-c) pyridine hydrochloride (PCA9), a tranquillizing agent (4, 2), on learning and memory traces were also studied.

MATERIALS AND METHODS

The method employed to study the effect of chlorpromazine, reserpine and PCA9 on learning and memory traces was essentially the same as described by Buresova et al. (3). This consisted of a simple one-trial learning procedure which was originally proposed by Kurtz and Pearl (6).

The apparatus consisted of a large wooden compartment (16×16×8 inches) connected by an opening (2.5×2.5 inches) to a small compartment (4.5×4.5×8 inches). The small compartment had an electrifiable grid floor. The opening between the large and small compartments had a removable transparent shutter.

In the present investigation 128 naive rats (100-130 g), of either sex, divided into 16 groups (8 in each) were employed. These animals had free access to food and water except during the experiment, and were used only once.

Experimental Procedure : A naive rat was placed into the large compartment and was allowed to explore the apparatus for 180 seconds. During this period the opening between the two compartments was kept open. The time spent in the small compartment was recorded with a stop watch (during the entire experiment only two rats did not enter the small compartment and these were replaced by two new rats). The opening between the two compartments was

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then closed and the rat was placed in the small compartment where it received painful electric shocks (1 msec, 8/sec, 30v), for 60 seconds, delivered to the grid floor by an electronic stimulator. This was the learning procedure.

The retention of the memory of painful stimuli, established in the learning procedure, was tested 24 or 48 hours later when the rat was allowed to explore the compartments for 180 seconds again in the absence of painful stimuli. Normally rats avoided entering the small compartment where they had received electric shocks. This change in behaviour has been termed as 'passive avoidance reaction' (3).

Drugs were tested at a dose level which did not affect motor coordination (using 'rotarod' test ED50 of PCA9, chlorpromazine and reserpine with respect to the impairment of motor coordination were found to be 168.4, 6.3 and 4.0 mg/kg, i.p. respectively (2). PCA9 (25 mg/kg), chlorpromazine (1 mg/kg) and reserpine (0.5 mg/kg) were injected intraperitoneally 15 minutes, 1 hour, 3 hours respectively before unconditioned exploratory behaviour and learning or retention test in order to see their effect on learning or retrieval. In order to study the effect on the consolidation phase of memory, PCA9 was injected immediately after learning while chlorpromazine was given just before learning and reserpine 30 minutes before learning because of their delayed onset of action. To see the effect on permanent memory, rats were treated 24 hours after learning and then put to retention test at 48 hours. With each set of experiment a control (saline) group was kept. The effect of compounds on learning and memory traces was assessed by comparing the mean time spent by the group of rats in the small compartment before shock and during retention test. The data was subjected to statistical analysis. The significance of differences from the control (saline) was found out by 't' test while the difference between the drugs were tested by the analysis of the variance.

RESULTS

Effects of PCA9 (25 mg/kg), chlorpromazine (1 mg/kg) and reserpine (0.5 mg/kg) on passive avoidance reaction in rats have been shown in Fig.1. The figure indicates mean time, in seconds, spent in the small compartment before the shock was applied and during retention tests. The vertical lines indicate the standard error.

In the present investigation it was observed that naive rats, when placed in the apparatus entered the small compartment within a few seconds and spent an average 140 seconds out of 180 seconds of the exploratory period (The difference between the mean time spent by different groups of rats in the small compartment before shock, i.e. during exploratory period, was insignificant). During the retention test saline treated rats spent on average only 23 seconds in the compartment. During the experiment it was observed that a few rats after spending a few seconds in the small compartment came out, spent a few seconds in the large compartment, and then re-entered the small compartment. In such cases the time spent in large compartment was subtracted.

PCA9 (25 mg/kg), chlorpromazine (1 mg/kg) and reserpine (0.5 mg/kg) did not influence the unconditioned exploratory behaviour of the naive rats. Groups of rats which learnt the
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There it received painful electric shocks from an electronic stimulator. The animal was trained in the learning procedure, was divided into the compartments for 180 seconds. It entered the small compartment during this period. The behaviour has been termed passive avoidance reaction under the effect of PCA9, chlorpromazine and reserpine spent on average 137, 132 and 117 seconds respectively in the small compartment during the retention test (Fig. 1). Rats, injected with PCA9 chlorpromazine and reserpine before the retention test, spent on average 113, 112 and 99 seconds respectively in the small compartment (Fig. 1). In groups where PCA9, chlorpromazine and reserpine were tested for their effect on the phase of memory traces, it was found that rats, during retention test, spent on average 92, 99, and 103 seconds respectively in the small compartment (Fig. 1). Rats injected with PCA9, chlorpromazine and reserpine after 24 hours of learning (i.e. during the phase of permanent memory) spent on average 36, 44, and 56 seconds respectively in the small compartment during retention test conducted 48 hours after learning (Fig. 1).

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Fig. 1.

Showing the impairment, caused by PCA9, 25 mg/kg; CPZ (chlorpromazine), 1 mg/kg and RSP (reserpine), 0.5 mg/kg, on learning, retrieval, consolidation phase of memory traces and permanent memory in rats using one-trial learning procedure. The figure indicates the mean time (in seconds) with standard error (vertical line) spent by the group of rats in the small compartment before shock (exploratory period) and during retention test. 8 rats were used in each group.

The results show that PCA9, chlorpromazine and reserpine significantly (P< 0.01) impaired acquisition (learning) and the consolidation process of the memory traces (temporary memory), while no such marked effect on the permanent memory was observed; in case of reserpine some impairment was seen which was probably due to the long duration of action of reserpine. However, all the three drugs suppressed retrieval of passive avoidance reaction (P< 0.01). The differences between the effects of the three drugs were insignificant when tested by the analysis of variance.
The effects on passive avoidance reaction (one trial learning procedure) indicate that PCA9, chlorpromazine and reserpine suppressed learning and retrieval. These drugs impaired the consolidation process of memory traces but did not affect markedly the permanent memory traces, though a little impairment was seen in case of reserpine which may be due to its long duration of action. The impairment of acquisition (learning) by chlorpromazine and reserpine using different conditioning methods has been reported by several workers (1, 7). The study of drug effects on learning and memory trace formation involves the difficulty of specifying the exact age of a trace. In a learning situation where an animal has had a hundred trials, the relevant traces may go back only a few trials or very many. Use of a single trial learning procedure assures that a treatment is exerted upon a trace which is of precise age (5). The clearest expression of the consolidation—preservation theory of memory traces was given by Mueller and Pilzecker (quoted by Jarvick and Byck (5) ), who on the basis of rather meagre evidence, proposed that a stimulus leaves behind it, a rather unstable trace which gradually stabilizes with the passage of time, if it is not first destroyed by a variety of influences. Pauling (8) has described that it is likely that consciousness and ephemeral memory (reverberatory memory) involves electric oscillations in the brain, and that permanent memory involves a material pattern in the brain in part inherited by the organism (instinct) and in part transferred to the material brain from the electric pattern of the ephemeral memory. Evidence that the ephemeral memroy, with an effective life that is rarely longer than a few minutes, is electrical in nature is provided by a number of observations.

The present investigation has shown the advantage and suitability of one-trial learning procedure in the study of psychopharmacological agents on learning and memory traces. However, there is some difficulty in assessing the effect of drugs, which have delayed onset of action, on the temporary memory traces.

SUMMARY

1-(β-phenylethyl) triazolo (4, 5-c) pyridine hydrochloride (PCA9), chlorpromazine and reserpine were found to suppress learning and retrieval of the passive avoidance reaction (one-trial learning procedure) in rats. In this test situation drugs impaired the consolidation process of memory traces but did not affect the permanent memory.

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REFERENCES


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