the threshold of EEG arousal reaction caused by hypothalamic stimulation, it only elevated the stimulation threshold of the reticular activating system, while sham rage and olfactory response were inhibited by the drug.

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# EFFECTS OF CENTRALLY ACTING DRUGS ON ACQUISITION OF A PASSIVE AVOIDANCE REACTION IN THE RAT

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The apparatus used was essentially that described by KURTZ AND PEARL[2]. It consisted (Fig. 1) of a large well-lit box connected to a smaller, dark compartment. Naive male rats placed in the large compartment tended to withdraw into the smaller one. The total time allowed in the apparatus was 2 minutes and at the end of this time the rat was enclosed in the smaller box and shocked through its feet. When re-introduced

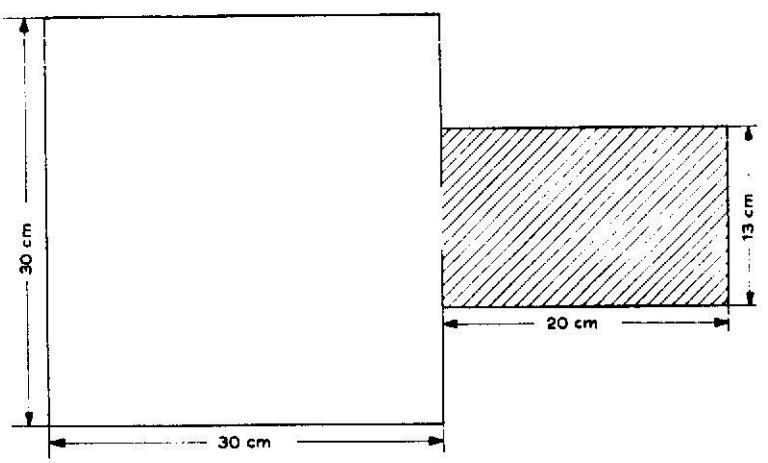


Fig. 1. Diagram of apparatus used.

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into the apparatus 24 hours later there was a tendency to avoid entry into the smaller box.

The effects of drugs upon the acquisition of this passive avoidance reaction were studied by administering the drugs by injection to the rats at such times that the peak effects were exerted at the time of the shock. Results of a typical experiment are shown in Figure 2 where 100 μg/kg LSD 25 produced some block of acquisition of the avoidance reaction without affecting the responses of rats which had not been shocked.

Other drugs shown to affect this acquisition (Fig. 3) were phencyclidine (2 mg/kg, 30 min before shock) and chlorpromazine (1 mg/kg, three and a half hours before shock).

The exact actions of the above-mentioned drugs on the brain are not clearly understood, so discussion of these results is difficult.

Figure 4 illustrates results from experiments with atropine sulphate (100 mg/kg, 30 min before shock) and N-methyl-3-piperidyl benzilate (2 mg/kg, 30 min before shock). Both these substances are anticholinergic in their action and both produced definite block of the acquisition of the avoidance reaction. Similar results have been reported by MEYERS *et al.*[3] with scopolamine and *l*-hyoscyamine and by BUREŠOVÁ *et al.*[1] with atropine sulphate. Atropine sulphate exerted its most marked effect when injected 30 minutes before shock (Fig. 5). At this time after injection other responses

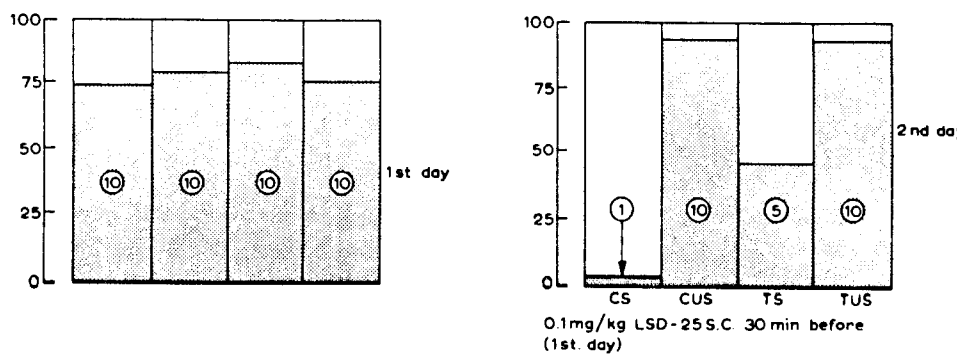


Fig. 2. Effect of LSD 25 on acquisition of passive avoidance reaction. 0.1 mg/kg LSD 25 s.c. 30 min before shock (1st. day). CS = Control shocked. CUS = Control not shocked. TS = Treated shocked. TUS = Treated not shocked.

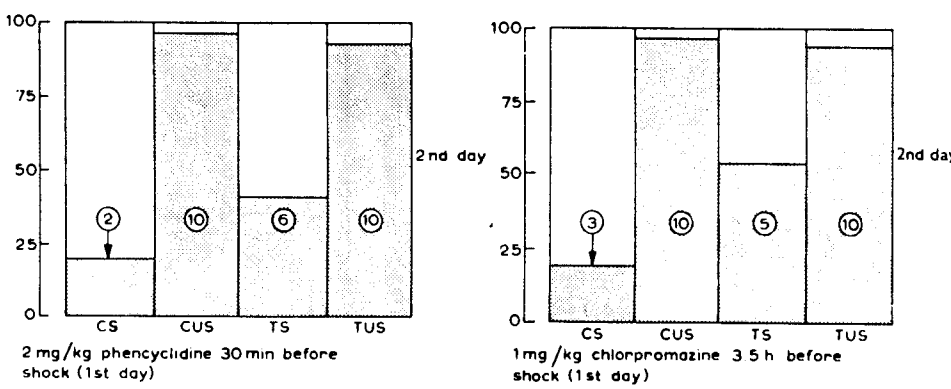


Fig. 3. Effects of phencyclidine and chlorpromazine on acquisition of passive avoidance reaction.

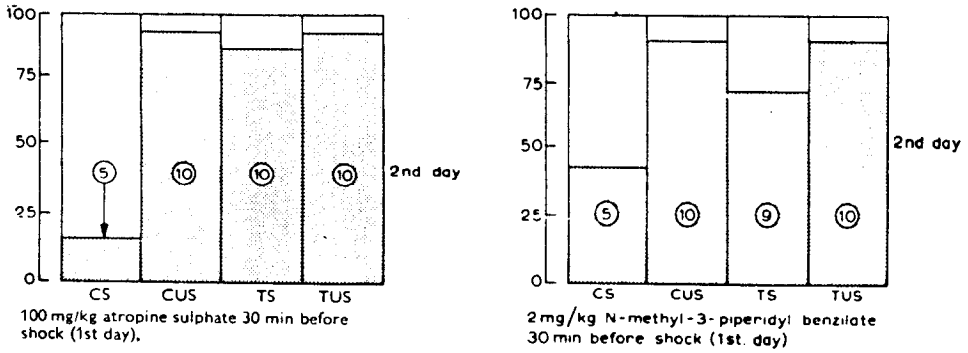


Fig. 4. Effects of atropine sulphate and N-methyl-3-piperidyl benzilate on acquisition of passive avoidance reaction.

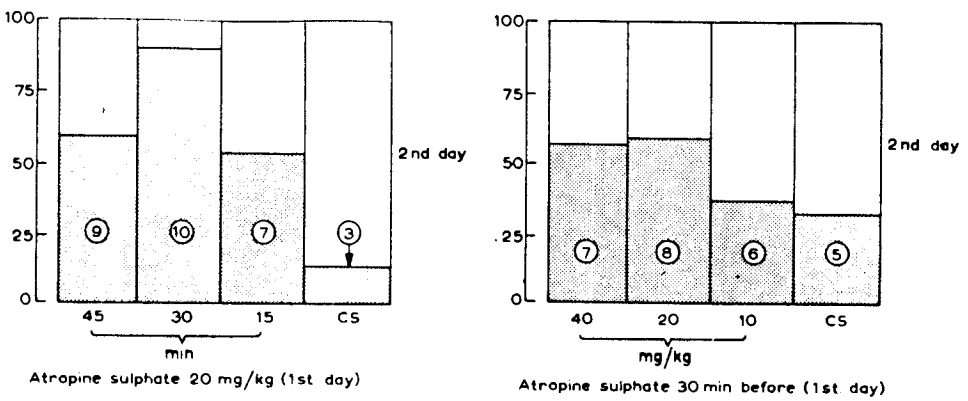


Fig. 5. Effects of atropine sulphate injected at different times before shock and in different doses on acquisition of passive avoidance reaction.

to atropine (*e.g.* mydriasis) were most marked, so presumably the effect of the atropine (having its peak effect at the time of shock) was on the acquisition of the response rather than on its retention.

If atropine and similar drugs blocked acquisition of the avoidance response by virtue of their anticholinergic action then facilitation of the acquisition might be expected to be produced by stimulation of muscarinic cholinergic activity. This was achieved indirectly by giving the anticholinesterase sarin (Fig. 6) and at a dose of 0.015 mg/kg there was some tendency for increased acquisition of the response. With physostigmine, however, no such facilitation occurred (Fig. 7) and direct increase in cholinergic activity achieved by administering oxotremorine, a muscarinic substance known to produce central effects, likewise had little or no effect on the acquisition of the response.

The results indicated that it was possible to interfere with acquisition of a passive avoidance response under the conditions described by administration of a number of centrally acting drugs. Anticholinergic compounds appeared to be particularly effective and there was some slight evidence for facilitation of acquisition of the response when central cholinergic activity was increased.

*References p. 336*

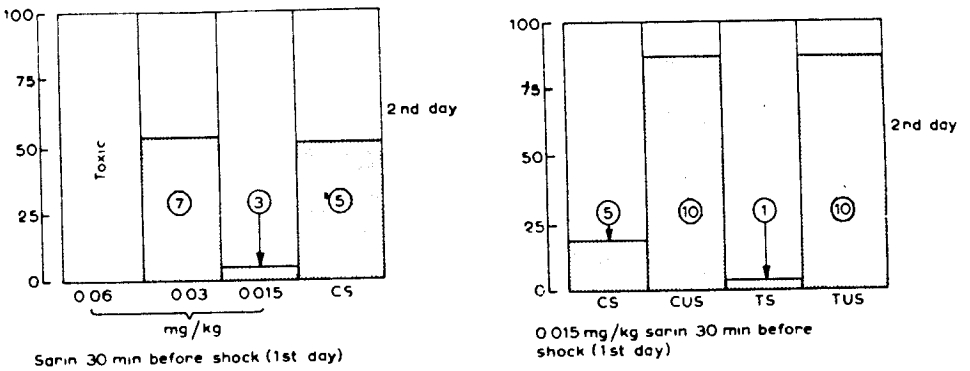


Fig. 6. Effects of sarin on acquisition of passive avoidance reaction.

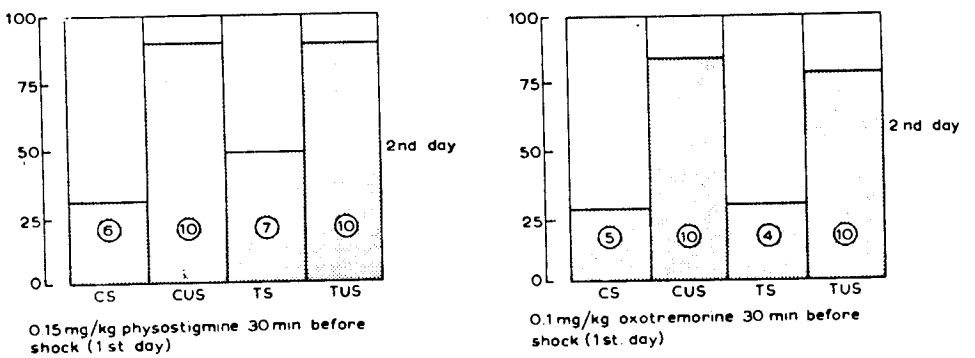


Fig. 7. Effects of physostigmine and oxotremorine on acquisition of passive avoidance reaction.

If this situation can be related to the learning or memory process, and this is not necessarily the case, it would seem most likely that the drugs affected the stage of perseveration rather than the stage of consolidation and the results would not be at variance with the idea[4] that learning efficiency depends on the ratio of acetylcholine to cholinesterase in the central nervous system.

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