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# Effect of Some Cholinergic Drugs on the Conditioned Pole Jump Response in Rats

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BHARGAVA, V. K. AND C. P. PUSHPAVATI. *Effect of some cholinergic drugs on the conditioned pole jump response in rats.* PHARMAC. BIOCHEM. BEHAV. **15**(4) 537–538, 1981.—Rats were trained to pole jump to a buzzer as the conditioned response. Cholinergic agents, oxotremorine and physostigmine significantly depressed this response. The effect was blocked by atropine. Nicotine and carbachol failed to modify the conditioned pole jump response. It is suggested that the central muscarinic inhibitory receptors are involved in the action of these drugs.

Conditioned avoidance  Cholinergic drugs  Conditioned pole jump response  Oxotremorine
Physostigmine  Atropine  Nicotine  Carbachol  Muscarinic receptors

THE involvement of the central cholinergic mechanisms in learning and memory has been extensively investigated; however, their precise role is still not well established [5]. Muscarinic cholinergic drugs have been shown to depress conditioned (pole jump) responses in rats [4], while anti-acetylcholine drugs produce a facilitation [2,3]. These effects appear to be related to the levels of acetylcholine in the brain [6]. Nicotine has been reported to produce variable effects: facilitation or depression of these responses [5].

The present study was therefore attempted to evaluate the role of cholinergic mechanism in acquisition of the pole jump response in rats with a view to assess the nature of the receptors involved in this mechanism.

## METHOD

Albino rats (150–200 g) of either sex were trained to acquire the pole jump response to conditioned and unconditioned stimuli as described by Rosecrans *et al.* [6]. The training sessions were conducted 4 sessions per week for 5–6 consecutive weeks before any drug was administered. Such animals showed 95–100% avoidance behaviour. Each animal was pre-treated with atropine methyl nitrate (2 mg/kg IP, 30 min) or atropine sulphate (2 mg/kg IP, 60 min) prior to the administration of cholinergic drugs. Such pre-treatments were found suitable in our earlier studies [1]. Following pre-treatment, each animal was placed in the behavioural box and given fifty trials. The average of these was taken as the pre-drug control (base line 100%) for each animal, and was compared with the average obtained after administration of test drugs.

Drugs dissolved in saline were administrated intraperitoneally (IP) and modifications in the pole jump response to the conditioned stimuli were recorded at frequent intervals to study the time course of the effect of different concentrations of drugs. The results were calculated as percent change in the pole jump response from the control value for each rat. A minimum of 4–6 experiments were carried out with each dosage of drug which were randomised. The level of significance was calculated using Student's *t*-test. Those animals which did not respond to the conditioned stimuli were subjected to unconditioned stimuli to study the effect of drugs on an escape response. In 4 preliminary experiments the effect of atropine methyl nitrate (2 mg/kg) was studied alone. In none of the experiments did atropine methyl nitrate modify the conditioned or unconditioned pole jump responses.

In order to exclude the possibility of involvement of skeletal muscles in the drug response, animals were tested for their muscle power by balancing them on a rotating rod before and after administration of drugs.

The drugs used included Physostigmine sulphate (eserine); atropine sulphate; carbamyl choline chloride (carbachol); nicotine (Sigma Chemicals); atropine methyl nitrate and oxotremorine (ICN Pharmaceuticals). The dosages were calculated as base for each drug.

## RESULTS

### *Oxotremorine*

10, 20, 50 and 100 μg/kg oxotremorine progressively depressed the pole jump response to the conditioned stimuli (Table 1). The effect of oxotremorine usually reached its peak within 15 min and lasted over 2 hrs after the administration of the drug. The onset and duration of the effect was related to the doses of oxotremorine. Figure 1 shows the time course effect of different concentrations of oxotremorine on the conditioned pole jump response. All animals responded to unconditioned stimuli.

### *Physostigmine (Eserine)*

0.05, 0.1 and 0.2 mg/kg physostigmine also depressed the conditioned pole jump response (Table 1). The maximum effect was seen within 15 min of administration and lasted

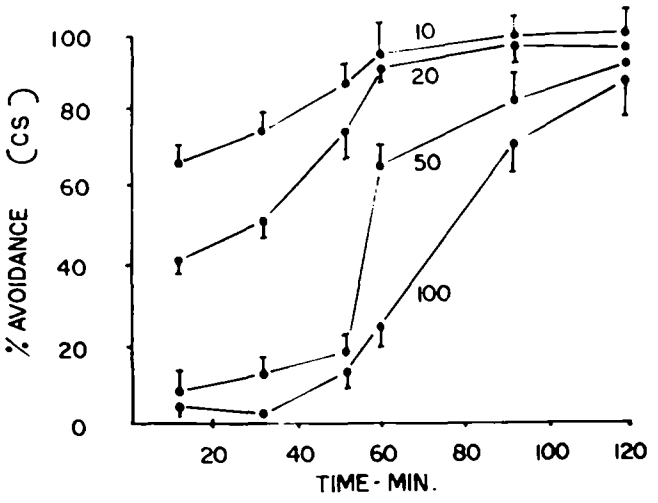


FIG. 1. Effects of oxotremorine (10,20,50 and 100 μg/kg.) on the conditioned pole jump in rats. Each point is an average ±S.E. of 4–6 experiments. The results are expressed as percent change of pre-drug control.

over 3 hrs. The escape response to unconditioned stimuli was not altered by physostigmine.

*Carbamyl Choline Chloride (Carbachol)*

0.5, 1.0 and 2.0 mg/kg carbachol did not modify the pole jump response to conditioned or unconditioned stimuli (Table 1). Carbachol invariably produced red tears in rats and occasionally salivation.

*Nicotine*

20, 30 and 50 μg/kg nicotine, like carbachol also failed to modify the pole jump responses to the conditioned or unconditioned stimuli (Table 1).

In order to study if muscarinic cholinergic receptors were involved in the drug action, animals were pre-treated with atropine sulphate (2 mg/kg IP), 60 min before the administration of the cholinergic drugs. Prior treatment with atropine, blocked the depressant effect of oxotremorine and physostigmine on the conditioned pole jump response. Table 1 summarises the results. Atropine on its own had no effect on the pole jump response.

TABLE 1

EFFECT OF DRUGS ON CONDITIONED AVOIDANCE RESPONSE

| Drug/kg | No. of Experiments | % Inhibition of Control (Mean ± S.E.) | % Inhibition after Atropine Pretreatment (Mean ± S.E.) |
|---|---|---|---|
| Oxotremorine | | | |
| 10 μg | 4 | 66.6 ± 12.8 * | 96.4 ± 8.2† |
| 20 μg | 6 | 40.8 ± 8.42* | 90.0 ± 10.4† |
| 50 μg | 6 | 8.3 ± 2.40* | 52.2 ± 6.4† |
| 100 μg | 6 | 6.3 ± 2.80* | 40.0 ± 4.2† |
| Physostigmine | | | |
| 0.05 mg | 6 | 70.0 ± 10.4* | 98.4 ± 10.8† |
| 0.10 mg | 6 | 58.6 ± 8.6* | 90.2 ± 16.4† |
| 0.20 mg | 6 | 26.6 ± 4.6* | 85.2 ± 12.2† |
| Carbachol | | | |
| 0.50 mg | 4 | 96.8 ± 20.8 | |
| 1.0 mg | 5 | 92.7 ± 24.8 | |
| 2.0 mg | 5 | 88.9 ± 16.2 | |
| Nicotine | | | |
| 20 μg | 5 | 92.6 ± 19.8 | |
| 40 μg | 5 | 90.8 ± 24.6 | |
| 50 μg | 5 | 86.5 ± 35.7 | |

Results are expressed as Mean (±S.E.) of percent change in conditioned avoidance response from the control (pre-drug level 100%) and after pretreatment with atropine sulphate (= 100%).

*Significantly different from control, $p < 0.001$.

†Significantly different from drug treatment alone, $p < 0.001$.

## DISCUSSION

The present study supports the hypothesis of the role of cholinergic mechanisms in acquisition of the pole jump response in rats. Our study shows that the muscarinic cholinergic agents, oxotremorine and physostigmine, depress the conditioned pole jump response. This effect is blocked by atropine. Nicotine does not seem to modify these responses in our present study, although we have seen that these concentrations of nicotine act centrally and modify the brain stem far-field potentials [1]. Carbachol also failed to modify the conditioned pole jump response. This may be due to an insufficient concentration of drug reaching the central receptors, as a result of poor penetration of the blood brain barrier. Since the effect of oxotremorine and physostigmine occur in animals pre-treated with atropine methyl nitrate, it is suggested that the modification of the pole jump response is due to a central action of these drugs. The unchanged motor activity simply points out that the depression of the pole jump response is not due to an action on the skeletal muscles.

In conclusion it appears that the depression of the acquisition of the pole jump response in rats is mediated by the central muscarinic cholinergic mechanisms. The possible role of other putative transmitters is under study.

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