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Effects of nicotine on motor co-ordination and spontaneous activity in mice

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Doses of nicotine (0·2 and 0·4 mg/kg subcutaneously) which depress spontaneous activity, improve the ability of mice to remain on a rotating rod, indicating that the reduction in activity is not due to non-specific disruption of motor ability.

The performance of rats trained to press a bar for water rewards is stimulated by small subcutaneous doses (0·05, 0·1 mg/kg) of nicotine; larger doses (0·2, 0·4 mg/kg) briefly reduce the rate of bar-pressing before increasing it (Morrison, 1967). The larger doses also depress spontaneous motor activity in mice (Morrison & Armitage, 1967). In the present experiments a rotating rod (Dunham & Miya, 1957) was used to test whether the depresssion of spontaneous activity caused by nicotine is a result of motor incapacity.

EXPERIMENTAL

Methods

Rotarod. Batches of 100 young male T.O. mice were trained to remain on a wooden rod 2 inches in diameter, rotating at a speed of 11 rev/min. Approximately 40% of the mice did not learn to stay on the rod at this speed and were rejected. The effects of nicotine were tested on the remaining mice with the rod rotating at 14 or 20 rev/min. At the slower speed most control mice could stay on the rod for 5 min or more but at 20 rev/min most fell off within 5 min. An improvement or impairment of performance could therefore be detected. The mice were tested 3 at a time; two of the animals were injected subcutaneously with nicotine while the third control mouse received physiological saline. After a delay of either 2 or 5 min the mice were placed on the rotarod and the time for which each mouse remained on the rod was recorded. After 5 min any mice remaining on the rod were removed.

Motor activity. This was recorded in boxes measuring 24 × 36 cm fitted with 3 photoelectric cells (Rossum, 1962). The mice were placed singly in the boxes for 1 h and their activity allowed to subside. They were then removed and injected subcutaneously with saline or nicotine, returned to the boxes and their activity recorded for a further 30 min.

RESULTS

Table 1 shows the effect of nicotine on rotarod performance in five experiments. The control mice varied greatly in their ability to stay on the rod, some falling off almost immediately and others remaining for the full 5 min of the test period. The majority fell off between 10 and 40 s. The variability in performance was not related to body weight or to time of day. Because of scores within each group of mice were not normally distributed, means and standard errors have not been presented. Instead, the time at which half the mice in a group had fallen off was calculated and the

results have been analysed statistically using the non-parametric Mann-Whitney U test. In four groups of mice (Experiments 1, 2 and 4) nicotine significantly increased the time the mice remained on the rod. In only one group did the mice injected with nicotine show a slightly poorer performance than the corresponding control group (Experiment 3). In the earlier experiments the mice were tested 2 min after injection, but when it became apparent that the depression of spontaneous activity caused by nicotine was at its greatest between 5 and 10 min after injection (see below) the delay between injection and testing was increased to 5 min. In one experiment (no. 4) mice were tested either 2 or 5 min after receiving 0·4 mg/kg of nicotine. Both experimental groups showed a significant improvement over the controls but this was greater after the shorter delay.

Table 1. *Effects of nicotine (Nic) on the ability of mice to remain on a rod rotating at 20 rev/min*

Expt	Treatment (dose in mg/kg)	Time between injection and test	No. of mice	Time for half the mice to fall off (s)
1	Saline	2 min	20	16
	Nic 0·2	,,	20	55·5**
2	Saline	2 min	19	25
	Nic 0·1	,,	19	75
	Nic 0·2	,,	18	186*
3	Saline	2 min	18	40
	Nic 0·2	,,	18	61·5
	Nic 0·4	,,	18	30
4	Saline	2 min	20	21
	Nic 0·4	2 min	20	66***
	Nic 0·4	5 min	20	28·5*
5	Saline	5 min	20	23·5
	Nic 0·2	,,	20	28
	Nic 0·4	,,	20	47·5

* P <0·05, ** P <0·01, *** P <0·001 Statistical significance of difference between nicotine injected and corresponding control group. Mann-Whitney U test.

In order to test the effects of very high doses of nicotine, a group of mice were trained and tested at 14 rev/min. At this speed most of the control mice remained on the rod for the whole of the 5 min period. Doses of nicotine up to 3·2 mg/kg did not affect their ability to stay on the rod. At a dose of 6·4 mg/kg of nicotine the average

Table 2. *Mean activity scores of groups of mice tested singly in activity boxes after nicotine administration*

Treatment	No. of mice	Activity counts (frequency of breaking light beam) 0–5 min	5–10 min	10–15 min	15–30 min
Saline	22	88	64	48	156
Nicotine 0·2 mg/kg	22	62	35	35	131
Nicotine 0·4 mg/kg	22	64*	22***	24***	73***

Mann-Whitney U test * P <0·05, *** P <0·001 Statistical significance of difference between nicotine and saline injected groups.

time on the rod of 16 mice was reduced to 3 min. Eight of these mice had convulsions and 4 of them died; the remainder showed severe tremors.

Table 2 shows the effects on motor activity of 0·2 and 0·4 mg nicotine/kg. Nicotine reduced activity and this effect was most pronounced between 5 and 10 min after the injection. For the 0·4 mg/kg dose the reduction was highly significant ($P < 0{\cdot}001$).

DISCUSSION

Motor activity, when measured by the boxes used here, is depressed by nicotine in rats as well as mice (unpublished observations) and no consistent evidence for a stimulant action of nicotine has been found in these studies. Nicotine, however, has a biphasic action on bar-pressing behaviour, a period of increased response following the initial phase of depression (Wanner & Battig, 1966; Morrison & Armitage, 1967; Morrison, 1967). In contrast to its effect on motor activity as measured by the activity boxes, nicotine did not depress activity in the rotarod test, its only detectable effect being improvement of performance.

The reduction in activity caused by nicotine in the activity boxes is unlike the effect of amphetamine in the same test, but there are similarities in the actions of these two drugs on bar-pressing behaviour. Nicotine also resembles amphetamine in its effect on rotarod performance since it has been shown that amphetamine also improves performance in these tests (Plotnikoff, Reinke & Fitzloff, 1962). Nicotine, therefore, can either decrease or increase performance, and the nature of the effect depends on the test used. The reduction in spontaneous motor activity caused by nicotine does not appear to be the result of a non-specific depression since amounts of nicotine which depress activity actually improve performance on the rotarod.

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