Effects of Stimulants on Rotarod Performance of Mice

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This study has demonstrated that amphetamine and pheniprazine increased performance time of mice on the rotating rod, whereas the effects of caffeine were questionable.

SEVERAL reports in the literature have suggested that various stimulant drugs have differential effects on various motor coordination tasks. Studies in lower animals appeared to be limited and it seemed of interest to evaluate the effects of various stimulant drugs on motor coordination. The present study will attempt to describe the effects of a group of stimulants on the performance of mice on a rotating rod, a test originally reported by Dunham and Miya (1).

METHODS

The apparatus originally reported by Dunham and Miya (1) was modified in the following manner: the rod consisting of a 1-in. wooden dowel was divided into 10 equal spaces of 3.5 inches by plastic disks of 8 inches diameter. The rod is operated by a kymograph motor (Gorell and Gorell Monodrum) which has an adjustable speed. One end of the wooden dowel was fitted into the kymograph drive shaft and the other into a ball bearing (1 inch) supported by a vertical wooden support.

The actual testing procedure consisted of (*a*) training all animals by placing them on the rotarod for 6 minutes, (*b*) injecting the animals with drugs by the intraperitoneal route, and (*c*) 30 minutes following injection, observing the performance of the animals on the rotarod for 1 hour, or until they fell off.

RESULTS

Studies on control mice consisted of performance evaluation at three different rotarod speeds. The results are shown in Table I.

TABLE I.—PERFORMANCE TIME *vs.* SPEED

Rotarod Speed, r.p.m.	No. of Groups of Mice[a]	Average Performance Time ± S.E., min.
A 29.28	10	24.5 ± 3.0
B 18.30	5	28.9 ± 4.1
C 11.44	16	30.2 ± 2.2

[a] Ten mice per group.

Although the mean performance times of the mice at the three speeds did not appear to differ significantly, gross differences in behavior were noted. The animals tested at the A speed were observed to have difficulty keeping up with the speed of the rod while those tested at the C speed spent a great deal of time in exploratory behavior. Thus, mice dropping off the rotarod at the A speed may be said to do so from failure to "keep up" with the rod, while those tested at the C speed dropped off primarily because of errors in exploratory behavior—attempts to climb or lean against the plastic disk dividers and/or side excursions on the rod itself. The behavior of the mice tested at the B speed resembled those tested at the A speed.

The effects of amphetamine on performance time were evaluated on three different rotarod speeds, A, B, and C. The results are shown in Table II.

The data shown would indicate that there is a dose response relationship with the use of amphetamine at the three speeds. The estimated doses effective in enhancing performance in 50% of the animals (ED_{50}) were found to be 2.8 ± 0.4 mg./Kg. for the A speed, 1.9 ± 0.4 mg./Kg. for the B speed, and 5.1 ± 0.5 mg./Kg. for the C speed ("estimated" ED_{50} only, since upper ratio was 1.48 at 5.0 mg./Kg.). Thus, there is no apparent difference (by inspection of means and standard errors) between the effects of amphetamine on A and B speeds; however, the agent is less active at the C speed.

The effects of pheniprazine also were evaluated at the three speeds and the results are shown in Table III.

Significant increases in mean performance time with the use of pheniprazine were observed in all three speeds. However, at the C speed the agent was seemingly ineffective 30 minutes after administration (standard error limits compared to controls) but had a pronounced effect at 2 hours. The estimated ED_{50} doses are 6.0 ± 0.8 mg./Kg. for the A speed, 7.0 ± 1.3 mg./Kg. for the B speed, and 6.5 ± 0.8 mg./Kg. for the C speed.

Caffeine was also evaluated at the three speeds and the results are shown in Table IV.

There was no significant improvement in the performance of mice treated with caffeine at any speed tested.

DISCUSSION

The present investigation has demonstrated that the stimulants, amphetamine and pheniprazine, enhance the performance of mice on the rotarod, whereas caffeine was found to be inactive or to have a questionable effect.

It is debatable whether this enhancement is due to a decrease in errors of judgment in movement or an actual improvement in muscular coordination. Thus, control animals tested at the C speed exhibited exploratory behavior while those tested at the A and B speeds did so to a much smaller extent.

Following medication, the animals appeared to concentrate to a greater extent on maintaining pace with the rotating rod and spent less time in exploratory behavior. Several reports indicate that amphetamine reduces errors in the performance of

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TABLE II.—EFFECT OF AMPHETAMINE ON PERFORMANCE

Speed	Dose, mg./Kg.	No. of Groups of Mice[a]	Mean Performance Time ± S.E., min.	Performance Ratios[b]
A	Controls	10	24.5 ± 3.0	1.00
	2.5	1	34.3 ± 7.3	1.40
	5.0	1	50.0 ± 1.0	2.04
	10.0	1	33.5 ± 8.0	1.36
B	Controls	5	28.9 ± 4.1	1.00
	1.25	1	37.0 ± 0.3	1.28
	2.5	1	51.3 ± 8.4	1.77
	5.0	1	52.5 ± 4.2	1.81
C	Controls	16	30.2 ± 2.2	1.00
	1.25	1.5	29.1 ± 9.4	0.96
	2.5	3.5	33.1 ± 2.5	1.09
	5.0	3.5	44.7 ± 4.9	1.48

[a] Ten mice per group. [b] Experimental/control.

TABLE III.—EFFECT OF PHENIPRAZINE ON PERFORMANCE

Speed	Pretreatment Time, hr.	Dose, mg./Kg.	No. of Groups	Mean Performance Time ± S.E., min.	Performance Ratios[a]
A	1/2	Controls	10	24.5 ± 3.0	1.00
		2.5	1	31.7 ± 16.7	1.29
		5.0	1	29.6 ± 12.7	1.20
		10.0	1	53.9 ● 6.2	2.19
B	1/2	Controls	5	28.9 ± 4.1	1.00
		2.5	1	29.4 ± 4.0	1.01
		5.0	1	43.1 ± 6.8	1.49
		10.0	1	44.6 ± 17.2	1.54
C	1/2	Controls	16	30.2 ± 2.2	1.00
		2.5	1	26.1 ± 12.7	0.86
		5.0	1	42.4 ± 10.0	1.40
		10.0	1	36.5 ± 8.7	1.20
C	2	Controls	16	30.2 ± 2.2	1.00
		2.5	0.5	37.7 ± 10.1	1.24
		5.0	1	43.3 ± 0.2	1.43
		10.0	2	47.2 ± 7.7	1.56
		20.0	0.5	60.0 ± 0.0	1.98

[a] Experimental/control.

TABLE IV.—EFFECT OF CAFFEINE ON PERFORMANCE

Speed	Dose, mg./Kg.	No. of Groups	Mean Performance Time ± S.E., min.	Performance Ratios[a]
A	Controls	10	24.5 ± 3.0	1.00
	5.0	1	12.9 ± 0.6	0.53
	10.0	1	18.2 ± 0.1	0.74
	20.0	1	6.6 ± 1.0	0.27
B	Controls	5	28.9 ± 4.1	1.00
	5.0	1	30.9 ± 4.2	1.07
	10.0	1	29.3 ± 7.3	1.01
	20.0	1	36.3 ± 1.6	1.27
C	Controls	16	30.2 ± 2.2	1.00
	5.0	1	30.1 ± 2.0	1.00
	10.0	1	26.3 ± 2.15	0.87
	20.0	1	32.5 ± 2.60	1.08

[a] Experimental/control.

repetitive tasks and improves muscular coordination in human subjects (2). Thus, this bioassay may be useful in characterizing the effects of other stimulants on motor coordination.

REFERENCES

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