The effects of magnesium pemoline, caffeine and picrotoxin on a food reinforced discrimination task¹

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The effects of several doses of magnesium pemoline, caffeine, and picrotoxin on the acquisition of a food-reinforced light-dark discrimination task in the T-maze were compared. Both magnesium pemoline and caffeine facilitated the acquisition of the task at appropriate doses. The picrotoxin-treated animals were incapacitated except at the lowest dose administered.

Magnesium pemoline has been shown to facilitate the acquisition of tasks motivated by both positive and negative reinforcement (Lubar et al, 1967; Kulkarni, 1967). Although magnesium pemoline is known to be a mild central nervous system (CNS) stimulant, several studies have shown that it also augments RNA polymerase production (Glasky & Simon, 1966; Simon & Glasky, 1968). Behavioral evidence supporting the view that magnesium pemoline's mechanism of action is not simply that of a mild CNS stimulant was provided by Plotnikoff (1966). He demonstrated magnesium pemoline facilitated acquisition of a jump-out avoidance while methamphetamine did not. Morris et al (1967) showed magnesium pemoline had no effect on RNA either in vivo or in vitro. Others have reported the behavioral effects of the drug are due only to CNS stimulant activity (Frey & Polidora, 1967; Beach & Kimble, 1967; Potts, 1968).

While a number of studies claim to have shown that magnesium pemoline's effect can be explained by CNS stimulation, only two published studies have compared magnesium pemoline and other CNS stimulants on the same task. Both studies utilized escape-avoidance paradigms. Plotnikoff (1966) found magnesium pemoline superior to methamphetamine and vehicle control groups in facilitating the acquisition of a jump-out avoidance task. Filby et al (1967) found that both magnesium pemoline and d-amphetamine enhanced the acquisition of a discriminated avoidance response; however, the magnesium pemoline treated group displayed fewer intertrial interval responses. When compared to CNS stimulants, the magnesium pemoline treated animals have shown superior acquisition of an avoidance response.

Comparisons of magnesium pemoline to other CNS stimulants on tasks utilizing positive reinforcement have not been reported. The present experiment was conducted to provide evidence concerning the effects of magnesium pemoline, caffeine, and picrotoxin on the acquisition of a positively reinforced light-dark discrimination in the T-maze.

METHOD

Forty-five naive male hooded rats raised and maintained under continuous light conditions were food deprived to 80% of their ad lib body weight and randomly assigned to 1 of 15 treatment conditions. All animals were between 110 and 130 days of age at the time of testing.

The apparatus consisted of a T-maze constructed of 3/8-in. plywood painted flat gray with a clear Plexiglas top and a grid floor throughout. The width of all the compartments was 6 in. and the depth from the grid floor to the top of the maze was 5 in. The startbox was 8 in. long and separated from the main alley of the maze by a guillotine door. The runway and arms of the maze were each 12 in. long. Lights (15 W) positioned behind translucent Plexiglas at each end of the runways served as the discriminanda for the task.

All drugs were suspended in a 0.3% tragacanth vehicle. Each S received an intraperitoneal (i.p.) injection of 5, 10, 15, or 20 mg/kg magnesium pemoline; 1, 3, 5, or 7 mg/kg caffeine; 0.25, 0.50, 0.75, or 1.00 mg/kg picrotoxin; or an equated volume of the vehicle. The S was then returned to the home cage and introduced into the maze 30 min later. Two minutes were allowed for adaptation after the animal was placed in the startbox.

All testing was done in a darkened room. The correct side was alternated from the left to the right arm of the T-maze according to a modified Gellerman sequence. As previous work done with rats from our colony raised under constant light conditions demonstrated that they had a distinct preference for the lighted arm of the maze (Potts, 1968), the darkened goal arm served as the correct stimulus. An incorrect trial was scored when the S placed both forepaws into the incorrect arm of the maze. As a correction procedure was used, every trial ended with a reinforcement which consisted of a 45-mg Noyes food pellet. A testing session terminated either when an animal performed to a criterion of nine correct responses in 10 trials or a S spent 15 min without consuming a pellet after leaving the startbox on any given trial.

RESULTS AND DISCUSSION

The animals treated with 1.0 mg/kg caffeine reached the 9/10 criterion in significantly fewer trials than the control group ($F = 4.66$, $df = 3/8$, $p < .05$), and the 10 mg/kg magnesium pemoline group also reached criterion in significantly fewer trials than the control group ($F = 5.35$, $df = 3/8$, $p < .05$). Animals treated at other dosage levels for both drugs did not differ from the control groups (Fig. 1).

None of the picrotoxin-treated animals dosed with 0.50 mg/kg or greater completed the task because they failed to consume the food pellet within the allotted 15-min interval

Fig. 1. The effects of various dosage treatments of caffeine and magnesium pemoline on the acquisition of a light-dark discrimination.

after leaving the startbox. The animals treated with 7 mg/kg caffeine and 20 mg/kg magnesium pemoline were also unable to complete the task in the allotted time.

These results suggest that magnesium pemoline's effect is not different from that of a CNS stimulant (caffeine) and both can facilitate the acquisition of a positively reinforced discrimination. The dose response effects for both drugs were nonlinear, showing an optimal dose for the facilitation of acquisition in our apparatus.

The failure of the picrotoxin-treated animals to run in the T-maze is at present unexplainable. Pretrial injections of the drug have been used successfully in an appetitive maze learning situation (Prien et al, 1963). McGaugh (1967) has stated that the effect of a given drug on learning varies with the drug dose, age, apparatus, strain, and sex of the animals used.

While several possible mechanisms such as stimulus reactivity (Beach & Kimble, 1967) or stimulant-enhanced consolidation (McGaugh, 1967) may explain the magnesium pemoline and caffeine data, more information of a comparative nature concerning the effects of both analeptics and RNA enhancers on learning is necessary.

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NOTES

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motivated, performed for its own sake rather than for some extrinsic goal (Koch, 1956). However, potential "extrinsic" incentives were present, i.e., auditory reinforcement from clicks produced by passage through the photocells, visual stimulation, handling, return to home cage, and feeding 1-h later. It is unlikely that such incentives produced the behavior because none were contingent on running.

Others have reported well-maintained, nonrewarded running. Clark & Miller (1966) found fast, nonrewarded running following rewarded runs in a T-maze and attributed their finding to use of a very short intertrial interval. In Logan's study (1960) of "operant-level" running in an alley, rats, given one trial a day, never failed to run, but their running was quite slow. Logan attributed the maintenance of running without reward to use of a very long intertrial interval, food deprivation, and confinement in small cages. The procedural differences between the present study and those of Clark and Miller, and Logan are too great to permit a statement concerning the conditions necessary to produce continued, nonrewarded running.

A feature of the present research is that it permits a comparison of the same gross response under rewarded and nonrewarded conditions. First, nonrewarded running can be as fast as rewarded running. Nonrewarded running is faster with a large endbox than with a small one, possibly because the large endbox permits more "playful" behavior. Second, because speeds were depressed for a large number of trials following food reward, fast nonrewarded running is probably not a case of positive transfer from prior reward conditions to nonreward

conditions. In the previously rewarded groups, the U-shaped function obtained on nonrewarded trials may reflect a change from "extrinsic" to "intrinsic" motivation. Third, speeds (and, from observation, the amount of "playful" behavior) on nonrewarded trials gradually increased, resembling an acquisition function obtained with reward, suggesting either the acquisition of S-R connections or increased incentive value with repeated experience. Fourth, peak performance without reward required many more trials to achieve than with reward, indicating either that the reinforcement for nonrewarded running is weaker than food reward, or that "intrinsic" motivation develops quite gradually. Fifth, terminal nonrewarded performance was unaffected by the previous schedule of reward. Perhaps the variables regulating "intrinsically"-motivated behavior are not the same as those regulating "extrinsically"-motivated behavior.

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NOTE

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