Magnesium pemoline: Effects on learning and retention in 250 day old rats

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The relative effects of pretrial injections of magnesium pemoline on learning vs performance was assessed in an avoidance situation utilizing 250 day old rats. The results were comparable to those using 90-120 day old rats. The drug appeared to have its major effect on performance through stimulant properties, but had no significant effect on learning.

Recent studies employing magnesium pemoline have suggested that the facilitation observed in avoidance conditioning may be due to the stimulant properties of the drug (Powell, Martin, & Kamano, 1967a, b) or to the drug's possible interference with freezing behavior (Frey & Polidora, 1967). Glasky & Simon (1966) suggest that magnesium pemoline is a CNS stimulant which stimulates brain systems known to synthesize RNA. According to Hyden (1961) RNA content first increases and then decreases with age, thus the age of the organism at the time of administration of magnesium pemoline is potentially an important variable.

The rats used in previous investigations have been between 90-120 days of age at the start of the experiments. The primary objective of the present study, following the basic design of Powell, Martin, & Kamano (1967a), was to investigate the effects of 20 mg/kg injections of magnesium pemoline in an avoidance situation utilizing older (250 days) rats.

METHOD

Subjects

The Ss were eight male, experimentally naive, Wistar rats obtained from the colony maintained at the Psychology Laboratory of the Galesburg State Research Hospital. Ss were 220-240 days of age, weighing between 375-500 g when brought to the Psychology Laboratory at Knox College. Ss were maintained for 30 days in individual cages, with ad lib access to food and water, prior to and during the study.

Apparatus

The apparatus used was a shuttle box measuring 23 in. long x 10½ in. wide and 11 in. high Plexiglas sides. It was divided into two compartments by a wooden partition. In the center of the partition was a guillotine door allowing access to the adjacent compartment over a 2½ in. hurdle. The ends of the box were constructed of aluminum on which two green panel lights were mounted, 6 in. above the floor and 2 in. from each side. The top was made of aluminum. A 1 mA shock from a Grason-Stadler shock generator-scrambler was delivered to the grid floor of the apparatus. A switching mechanism allowed either half of the box to be electrified. CS-UCS intervals and presentation was controlled by mechanical programming equipment which was activated when the guillotine door was raised at the beginning of a trial.

Procedure

The Ss were randomly divided into two groups by use of a table of random numbers, placebo (N = 4) and drug (N = 4), and handled for 5 min per day for three days prior to training. Following gentling, Ss were allowed to adapt to the apparatus for 10 min on two consecutive days. During the adaptation period, the guillotine door between compartments was raised. At the start of avoidance training, drug Ss received a 20 mg/kg injection of magnesium pemoline (suspended in 0.3% tragacanth, 10 mg/cc concentration) IP 40 min prior to being placed in the apparatus.² Placebo Ss received an equivalent injection of normal saline on the same time schedule. The Ss

were allowed to adapt to the apparatus (door open) for 2 min prior to the beginning of training. Avoidance conditioning consisted of 15 trials per day for four consecutive days. A trial was defined as light onset, door opening (CS) followed 5.0 sec later by shock. CS and UCS continued until S jumped the hurdle into the adjoining compartment. The intertrial interval approximated 30 sec. Crossing the hurdle prior to UCS onset was a conditioned avoidance response (CAR).

Testing sessions were begun 72 h after termination of training. The procedures employed were exactly the same as those used during training. The drug and placebo training groups were each subdivided into two groups, thus forming four testing groups; drug-drug (N = 2), drug-placebo (N = 2), placebo-drug (N = 2), and placebo-placebo (N = 2). The testing groups were matched, as nearly as possible, on the basis of avoidance performance during the last day of training. Mean last day training scores were 7.50, 9.00, 1.00, and 3.00, respectively.

RESULTS AND DISCUSSION

The mean number of CARs during training for drug and placebo Ss by days is presented in Fig. 1. An analysis of variance for repeated measures yielded a significant treatment effect ($F = 9.01$; $df = 1/6$; $p < .05$), and days effect ($F = 6.87$; $df = 3/18$; $p < .05$), but no significant treatment by days interaction ($F = 2.83$; $df = 3/18$; $p > .05$).

In order to take into account final level of training performance in the analysis of test performance, a difference score was utilized. The final level of performance was subtracted from each test day performance for each S. A constant was added to each difference score to eliminate negative scores. Mean performance difference scores by days are presented in Fig. 2. Prior to analysis, the scores were transformed ($X = \sqrt{X} + \sqrt{X+1}$) in an attempt to insure homogeneity of variance (Edwards, 1968). An analysis of variance of these transformed scores for repeated measures on the same Ss yielded no significant effect of treatment during testing, ($F = 0.95$; $df = 3/4$; $p > .05$); no significant effect of treatment during training on later test performance ($F = 2.13$;

Fig. 1. Mean CARs during acquisition for drug and placebo groups.

Fig. 2. Mean adjusted CARs during testing for each of four groups.

$df = 3/12$; $p > .05$); and no significant interaction ($F = 1.97$; $df = 9/12$; $p > .05$). An inspection of Fig. 2 does suggest that Ss receiving magnesium pemoline during the test period, perform at a higher final level than the placebo groups, however, as stated, the difference was not significant.

The results of the present study are in agreement with those of Powell, Martin & Kamano (1967a, b) and Frey & Polidora (1967) in that 20 mg/kg injections of magnesium pemoline facilitated acquisition of an avoidance response in rats, but had little or no effect on subsequent retention. The data presented suggests that magnesium pemoline administered to 250 day old rats, has a comparable effect to that obtained when using 90-120 day old rats, and suggests, as they have concluded that facilitation may be due to the stimulant properties of the drug or to the interference with freezing behavior.

REFERENCES

- EDWARDS, A. L. *Experimental design in psychological research*. (3rd ed.). New York: Holt, Rinehart and Winston, Inc., 1968.
- FREY, P. W., & POLIDORA, V. J. Magnesium pemoline: Effect on avoidance conditioning in rats. *Science*, 1967, 155, 1281.
- GLASKY, A. J., & SIMON, L. N. Magnesium pemoline: Enhancement of RNA polymerases. *Science*, 1966, 151, 702.
- HYDEN, H. Biochemical aspects of brain activity. In S. Farber and R. Wilson (Eds.), *Control of the mind*. Part 1. New York: McGraw-Hill, 1961.
- POWELL, B. J., MARTIN, L. K., & KAMANO, D. K. Magnesium pemoline: Effects of training vs testing of an avoidance response. *Psychonomic Science*, 1967, 8, 203-204.
- POWELL, B. J., MARTIN, L. K., & KAMANO, D. K. More on Magnesium pemoline: Differential effects of advance and immediate injections on avoidance performance. *Psychonomic Science*, 1967, 8, 303-304.

NOTES

1. The author thanks Hollis Schoepke of Abbott Laboratories for supplying the magnesium pemoline.
2. The author thanks Charles Lange of West Drug Company for placing the drug in suspension.