Magnesium pemoline: 'Effects of training vs testing of an avoidance response

BARBARA J. POWELL, L. K. MARTIN AND D. K. KAMANO

GALESBURG STATE RESEARCH HOSPITAL

The relative effects of magnesium pemoline on learning vs performance of avoidance conditioning were assessed. The drug appeared to exert its major effect on performance through stimulant properties, but had no significant effect on learning.

Initial work by Plotnikoff (1966a, b) with magnesium pemoline indicates that the drug not only enhances learning of an avoidance response in rats, but also memory for the task; however, these reports of the dramatic effectiveness of the drug have been criticized both from the standpoint of methodology and data interpretation (Bowman, 1966). Moreover, attempts of other investigators to substantiate the alleged effects of pemoline on both learning and memory have met with failure (Beach & Kimble, 1967; Frey & Polidora, 1967). This study was designed to assess the effects of magnesium pemoline on "learning" or training vs "performance" or subsequent testing of an avoidance response in rats, using each S as his own control.

Method

Ss were 45 experimentally naive male Wistar rats from the colony maintained at the Psychology Laboratory, Galesburg State Research Hospital. Ss were 100-125 days of age and during testing were maintained two per cage, with ad lib access to food and water.

Apparatus

The avoidance apparatus was a modified Miller-Mowrer jump box. The jump box, UCS, and CS are described in detail elsewhere (Powell, Martin, & Kamano, 1965).

Procedure

For avoidance training, Ss were divided into two groups, placebo (N=20) and drug (N=25). Drug Ss were injected IP with 20 mg/kg magnesium pemoline suspended in 0.3 percent tragacanth (10 mg/cc concentration) 40 min prior to each conditioning session, while placebo Ss received an equivalent injection of normal saline. Avoidance conditioning consisted of 15 trials per day for three consecutive days. Each trial consisted of light (CS) followed 5 sec later by shock (UCS, intensity=300 μ A). Both CS and UCS continued until S jumped the hurdle into the adjoining compartment. The intertrial interval averaged 30 sec and crossing the hurdle during the 5-sec CS-UCS interval constituted a conditioned avoidance response (CAR).

Testing, which occurred 72 h after termination of training, involved exactly the same procedure; how-

ever, the drug condition for some Ss from both the original drug and placebo groups was changed, thus forming four testing groups: drug-drug (N=5), drug-placebo (N=5), placebo-placebo (N=10), and placebo-drug (N=10),² which were matched on the basis of mean avoidance performing during training (mean training scores for these four groups were 16.60, 15.60, 8.20, and 8.10, respectively).

The general hypothesis with respect to avoidance performance during testing was as follows: If differences between drug and placebo Ss are found during training and if such differences are due to *learning*, changing drug condition during testing should be irrelevant to avoidance responding. Conversely, if drug effects are on *performance*, avoidance responding during testing will be determined by drug condition.

Results and Discussion

The mean number of CARs emitted during training for drug and placebo Ss is presented in the left half of Fig. 1. An analysis of variance of this performance (corrected for unequal N by unweighted means procedure (Winer, 1962)) revealed significant effects of drug ($F=5.36$, $p<.05$) and a drug by day interaction ($F=7.24$, $p<.01$), with drug effects manifested on the second day of training.

Mean performance by days for the testing period is presented in the right half of Fig. 1. Prior to analysis, these data were transformed ($X=\sqrt{x} + \sqrt{x+1}$) to insure homogeneity of variance. The analysis of

Fig. 1. CARs in training and testing for drug and placebo groups.

variance (corrected for unequal N) yielded no significant effects of drug condition during training ($F=0.82$), drug condition during testing ($F=2.44$), and no significant interaction ($F=2.03$). Relative to Ss for which drug was discontinued, Ss which continued to receive pemoline during testing (the D-D group) seemed to have better retention; however, as already noted, this difference was not significant.

In general, the results of the present study are in agreement with those of other investigators (Beach & Kimble, 1967; Frey & Polidora, 1967) in that 20 mg/kg injections of magnesium pemoline facilitated avoidance conditioning in the rat but had little or no effect on subsequent retention. The tendency for an increment in performance of Ss which received drug both during training and testing suggests that facilitation may be due to the stimulant properties of the drug and/or to the drug's possible interference with freezing behavior (Frey & Polidora, 1967).

Comment on Solyom, Beaulieu and Enesco by Hugh L. Evans

Solyom et al (1966) report that RNA-treated rats do not acquire a bar-pressing response more rapidly than control animals, but do show a higher rate of responding with extended training, and a subsequent resistance to extinction.

It is felt that the above authors failed to make use of some pertinent information in the interpretation of their results. First, it is reported that the RNA-treated group did not acquire the CR sooner than the controls. In addition, there appears to be no difference between RNA and control groups in the number of trials to asymptotic VI performance. Thus RNA rats were no more proficient, in terms of reinforcements earned, than controls. Similar data have been reported for operant conditioning with food as the reward (Brown, 1966). Second, with extended training RNA rats developed a higher response rate; but on a VI schedule high response rate is not a measure of learning or adequacy of performance. Many drugs (amphetamine, caffeine) enhance the tendency to respond but have no effects on learning (e.g., Weiss & Laties, 1962). Crucial information about effects on learning could be gotten by continued testing after RNA injections have ceased.

Finally, the extinction data show that animals responding at a high baseline rate generate extinction curves differing slightly from those with a lower

References

- Beach, G., & Kimble, D. P. Activity and responsivity in rats after magnesium pemoline injections. *Science*, 1967, 155, 698.
- Bowman, R. E. Magnesium pemoline and behavior. *Science*, 1966, 153, 902.
- Frey, P. W., & Polidora, V. J. Magnesium pemoline: effect on avoidance conditioning in rats. *Science*, 1967, 155, 1281.
- Plotnikoff, N. Magnesium pemoline: enhancement of learning and memory of a conditioned avoidance response. *Science*, 1966a, 151, 73.
- Plotnikoff, N. Magnesium pemoline: enhancement of memory after electroconvulsive shock in rats. *Life Sci.*, 1966b, 5, 1495.
- Powell, B. J., Martin, L. K., & Kamano, D. K. Effects of amobarbital sodium and meprobamate on acquisition of conditioned avoidance. *Psychol. Rep.*, 1965, 17, 691.
- Winer, B. J. *Statistical principles in experimental design*. New York: McGraw-Hill, 1962.

Notes

1. We thank Hollis Schoepke of Abbott Laboratories for supplying the magnesium pemoline.
2. Fifteen of the drug training Ss were used for another purpose and are not included in the testing data.

baseline rate. Because Solyom's results do not indicate a differential degree of learning during the training phase, the extinction evidence favors an RNA effect on performance, but not on learning. Evidence that RNA treatments produce no changes in open field activity has no bearing on this problem. In fact, Corson & Enesco (1966) report RNA to produce changes in instrumental performance that do not arise from the learning process. An additional group of animals trained under RNA but extinguished without RNA would establish the importance of RNA per se on rate of extinction. If learning were enhanced by an experimental treatment, subsequent behavioral indices of learning should be independent of continued treatment. In short, while the Solyom results are acceptable evidence for an RNA effect on performance, they offer no "suggestive evidence" for learning effects.

References

- Brown, H. Effect of ribonucleic acid on the rate of lever pressing in rats. *Psychol. Rec.*, 1966, 16, 173-176.
- Corson, J. A., & Enesco, H. E. Some effects on injections of ribonucleic acid. *Psychon. Sci.*, 1966, 5, 217-218.
- Solyom, L., Beaulieu, C., & Enesco, H. E. The effect of RNA on the operant conditioned behavior of white rats. *Psychon. Sci.*, 1966, 6, 341-342.
- Weiss, B., & Laties, V. G. Enhancement of human performance by caffeine and the amphetamines. *Pharmacol. Rev.*, 1962, 14, 1-36.