More on magnesium pemoline: Differential effects of advance and immediate injections on avoidance performance

BARBARA J. POWELL, L. K. MARTIN AND D. K. KAMANO
GALESBURG STATE RESEARCH HOSPITAL

Administration time was varied in an attempt to assess effects of magnesium pemoline on avoidance performance. Advance injections enhanced avoidance performance more than immediate injections, suggesting that facilitation of performance was due to either pemoline's stimulant action and/or to the fact that drug action is delayed.

According to Glasky & Simon (1966), magnesium pemoline is a mild central nervous system stimulant which is thought to stimulate brain systems known to synthesize RNA, an agent which has been linked to learning and memory (e.g., Hilgard & Bower, 1966). As noted by Morris, Aghajanian, & Bloom (1967), although Glasky and Simon declined to specify a causal relationship between stimulation of RNA and memory effects, they implied that magnesium pemoline might be used to investigate the possible existence of such a relationship.

If the primary action of magnesium pemoline is RNA synthesis rather than central nervous system stimulation, injection time is potentially an important variable. For example, consistent with the view that memory storage involves processes which are active after an experience occurs, several investigators have found that administration of certain drugs *after* a training session facilitates memory while others, even though facilitating performance, have no demonstrable effect on memory (Bovet, McGaugh, & Oliverio, 1966; Doty & Doty, 1966; Irwin & Benuazizi, 1966).

One method of distinguishing between possible stimulant or performance enhancing properties of drugs from those involved with retention is varying time of drug administration. The present study deals with the effects of advance vs immediate injections of magnesium pemoline on the avoidance performance of rats.

Method

Ss were 80 male Wistar rats. Ss and apparatus were identical with those described elsewhere (Powell, Martin, & Kamano, 1967). Forty Ss, divided into equal drug and placebo groups received injections of either magnesium pemoline suspended in 0.3 percent tragacanth (10 mg/cc concentration) or physiological saline 40 min prior to each conditioning session (which lasted about 12 min) while the remaining Ss, also divided into equal subgroups, received equivalent injections immediately prior to each session so that peak effect of the drug would occur shortly *after* each conditioning session.

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 μa). 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 an avoidance response.

Results and Discussion

The mean number of CARs emitted by drug and placebo Ss during training under conditions of advance (40 min) and immediate injection is presented in Fig. 1. An analysis of variance of this performance revealed significant effects of drug ($F = 10.23$, $p < .01$) and injection time ($F = 4.15$, $p < .05$), with virtually no interaction ($F = .06$). Ss receiving pemoline had better acquisition performance than placebos regardless of injection time; however, the number of avoidance responses for both drug and placebo Ss increased as a function of the advance injection procedure.

Of additional interest is the finding that performance of placebos also differed with advance and immediate injections of physiological saline. The su-

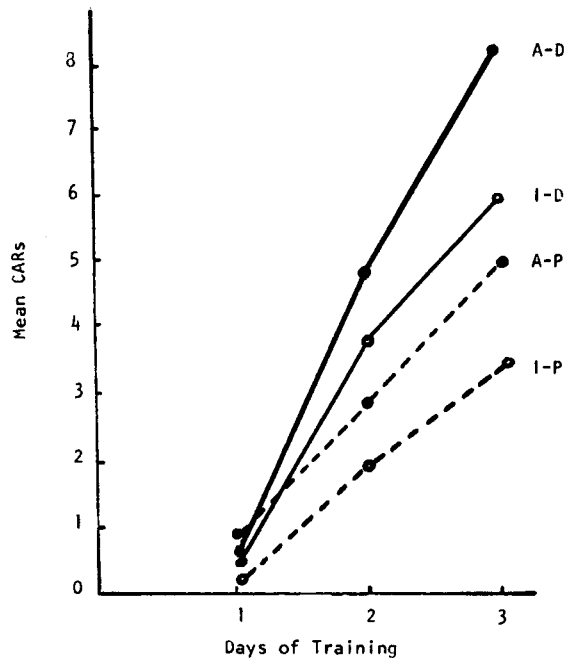

Fig. 1. Mean CARs during acquisition for advance drug (A-D), immediate-drug (I-D), advance-placebo (A-P), and immediate-placebo (I-P) injection groups.

perior CAR acquisition of Ss receiving *advance* injections of saline is in general agreement with another study (Schnitzer & Ross, 1961) which identified increased activity in mice as a possible effect of saline administration; however, since the overall effects of immediate injection were *identical* for drug and placebo groups, the decrement in performance (relative to the advance injection groups) may be due strictly to the injection time factor.

The finding that conditioning under magnesium pemoline was superior with advance injections tends to suggest that the stimulant properties of the drug were responsible for or related to performance increments; however, this alone does not explain the superiority of the immediate injection drug Ss over a comparable group of placebos. One possible explanation is that the stimulant properties of the drug were cumulative over the three days of training.

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