Magnesium pemoline: Facilitation and debilitation of heart rate classical discrimination conditioning in rabbits¹

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Oral administration of magnesium pemoline (10 mg/kg) 1/2 h prior to each training session enhanced heart rate discriminations in acquisition. When further acquisition training was given without the drug after a 14 day rest period, retention of the discrimination was debilitated in comparison with the control group.

Several studies using aversive stimulation have reported that magnesium pemoline (MP) has a mild stimulating effect upon performance (e.g., Beach & Kimble, 1967; Frey & Polidora, 1967; Plotnikoff, 1966). Findings in these studies, such as the report by Frey and Polidora that MP augments responsiveness in rats adopting a "freezing" posture, suggest that the drug may have an effect upon induced "emotional" components of behavior. In the present experiment heart rate (HR) and nictitating membrane (NM) responses were concomitantly conditioned in rabbits. Essentially the NM response in rabbits seems to be skeletally mediated (Lierse, 1960); whereas, HR decelerations are primarily due to compensatory vagal responses to blood pressure elevations induced by activation of the sympathetic nervous system (Yehle, Dauth, & Schneiderman, 1967). Although HR decelerations are not isomorphic with all indices of "emotional" responsiveness, sympathetic activation is generally considered to be related to fight or flight reactions.

Method

Each of 40 Ss was assigned to one of five groups receiving either an intraperitoneal (IP) injection of physiological saline, or oral administration of either a placebo or a capsule containing 5-, 10-, or 15-mg/kg of MP 1/2 h before each acquisition session. The group receiving IP injections of saline was included because preliminary observations suggested that oral intubation of a capsule directly into the esophagus by means of a catheter is aversive to rabbits. The oral route was chosen for administration of MP and its placebo control because the drug has only limited solubility in commonly used pharmacologic mediums.

The conditioning apparatus, methods of recording, and manner in which each S was restrained within a Plexiglas box have previously been described (Gormezano, 1966). Each S was given one day of adaptation under the drug to 550 and 3400 cps, .7 sec duration tones at 72 dB SPL followed by seven suc-

cessive days of classical conditioning (also under the drug). During conditioning sessions one of the tones was followed by a .3 sec duration, 5 mA ac shock to the lateral canthus of the right eye, and the other was not. Fourteen days later the S was given two more classical discrimination conditioning acquisition sessions, but without the drug. In each acquisition session the S received 76 trials at an intertrial interval of 85 sec. Thirty-three tone presentations were paired with shock each day, and five presentations of the same frequency tone presented alone served as test trials for the reinforced tone. Of the 38 nonreinforced tones, five presentations served as test trials for the nonreinforced tone.

Measures of HR change were obtained on test trials by dividing the interresponse time of the 10 successive beats after tone onset by the interresponse time of the 10 beats preceding tone onset; measures of NM were recorded on every trial. A measure of discrimination was obtained in each system by taking the difference in performance between responses to the reinforced and nonreinforced tones and dividing them by the responses to the reinforced tone. One-way analyses of variance in conjunction with Dunnett a posteriori t tests were conducted upon cumulated daily acquisition and discrimination scores. In addition, t test comparisons were made between the placebo and IP saline groups.

Results and Discussion

The major finding of the present experiment was that a 10 mg/kg dose of MP enhanced HR discriminations in acquisition, but debilitated retention of the discrimination when the Ss were given further acquisition training 14 days later without the drug (see Fig. 1). Statistical analyses confirmed that the 10 mg/kg drug group differed significantly ($p < .05$) from the oral placebo group in acquisition, but failed to confirm similar differences in the 5- and 15-mg/kg MP groups. After 14 days in their home cages, the control Ss continued to show improvement in HR discrimination when they were given further acquisition training without capsules. In contrast, the groups which had previously received MP before their acquisition sessions revealed poorer HR discriminations when they were later run without the drug. The greatest debilitation occurred in the 10 mg/kg drug group on the first day of being run without the drug. Differences in discrimination be-

tween this group and the oral placebo control group were reliable ($p < .05$). Interestingly, an examination of the tabular data presented by Frey & Polidora (1967) suggests that a similar performance enhancement under MP in their experiment was also followed by performance debilitation in the absence of the drug. In any event, these findings indicate the need for evaluating performance in non-drugged as well as drugged states when assessing the effects of pharmacological agents upon conditioning.

One conceivable explanation for the performance decrement in the present study is suggested by Estes' statistical learning theory (1959). According to this interpretation, aspects of S's internal state were influenced by MP and comprised a portion of the stimulus complex to which the S became conditioned. Subsequently, when the drug was withdrawn, the S's internal state was altered in such a way as to change the stimulus complex and debilitate performance in the conditioning situation.

In contrast to the facilitation of HR discriminations under the drug, neither NM acquisition nor discrimination scores revealed reliable differences between the MP groups and the oral placebo control group. However, the percentage of NM CRs observed in the

Fig. 1. Percentages of HR discrimination in each group during seven days of classical discrimination training under magnesium pemoline (acquisition) followed after 14 days of rest by two days of conditioning without the drug (re-acquisition). The inserted figure shows percentages of HR responses to the reinforced (CS+) and nonreinforced (CS-) tones during each day of acquisition and re-acquisition for the 10 mg/kg magnesium pemoline group compared with the oral placebo control group.

Fig. 2. Comparisons of oral (capsule) and intraperitoneal (saline injection) routes of administration upon measures of NM and HR responding to the reinforced tone.

oral placebo group was lower and revealed greater inter-S variability than in other of our experiments not employing the oral route. A comparison of the effects of oral and IP routes of administration upon NM and HR conditioning in the present experiment indicated that the oral route reliably ($p < .05$) debilitated NM conditioning; whereas HR responding to the reinforced tone, although higher in the oral than in the IP group (see Fig. 2), was not significantly enhanced.

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Note

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