Marijuana Enhancement of Shuttle-Box Avoidance Performance in Rats[1] (36829)

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Marijuana-induced disruption of previously established conditioned behavior has been demonstrated with various procedures including operant responding for food or water (1–5), rope climbing for food (5), maze running for food (6), and shuttle-box avoidance (6, 7). Carlini and Kramer (8) reported that administration of marijuana extract to rats before acquisition trials improved maze learning for food. However, Orsingher and Fulginiti (6), using essentially the same behavioral technique, observed disruption of acquisition by marijuana. The same investigators reported that chronic treatment with marijuana also impaired acquisition of shuttle-box avoidance (6). Park and Tilton (9) examined the effect of marijuana smoke on acquisition of shuttle-box avoidance by 3 strains of rats. They found that the avoidance responses of a strain which usually performed well were decreased while avoidances of poorly performing strains were increased. Their results were interpreted in terms of an effect of marijuana on learning and it was suggested that various strains repond differently to marijuana. We have observed that marijuana extract disrupts shuttle-box avoidance of rats which perform at the 80% level or higher (7). In our experiments, tolerance developed to the disruptive effect within 5–7 days. Approximately 50% of the strain of rats which we are using never achieve a shuttle-box avoidance level above 10% (hereafter, these rats are referred to as poor performers). Rech (10) has shown that amphetamine can improve the avoidance performance of this type of animal. Because marijuana administered repeatedly produces certain amphetamine-like effects (unpublished observations) we decided to (a) determine the effect of marijuana on shuttle-box avoidance of rats with a previously established base line of poor performance and (b) examine the influence of marijuana on acquistion of avoidance behavior.

Methods. A Lehigh Valley two-way shuttle-box was used in these experiments. Trials were initiated every 30 sec by a light activated on the side of the cage occupied by the rat. After 5 sec, a scrambled constant current shock (0.6 mA) was applied to the grids on that side of the cage for an additional 5 sec, after which the light and shock were terminated. If the animal moved to the unlighted side during the initial 5 sec, the response was scored as an avoidance, the light was terminated, and no shock was applied. A response during the second 5 sec terminated the light and shock and was scored as an escape. Female rats (250–300 g, Sprague-Dawley descent, Texas Inbred Mice Co.) were subjected to 80 trials/day, and drug or placebo was administered either 2 hr before or 5–15 min after sessions. Marijuana extract distillate (MED; generously supplied by Dr. Scigliano, NIMH) containing 17.1% Δ^9-THC was diluted with 6% Tween 80 in distilled water to a concentration of 20 mg/ml Δ^9-THC. The drug was administered orally via a polyethylene tubing passed into the stomach. The oral route of administration was chosen because previous studies had shown that repeated ip injections produced

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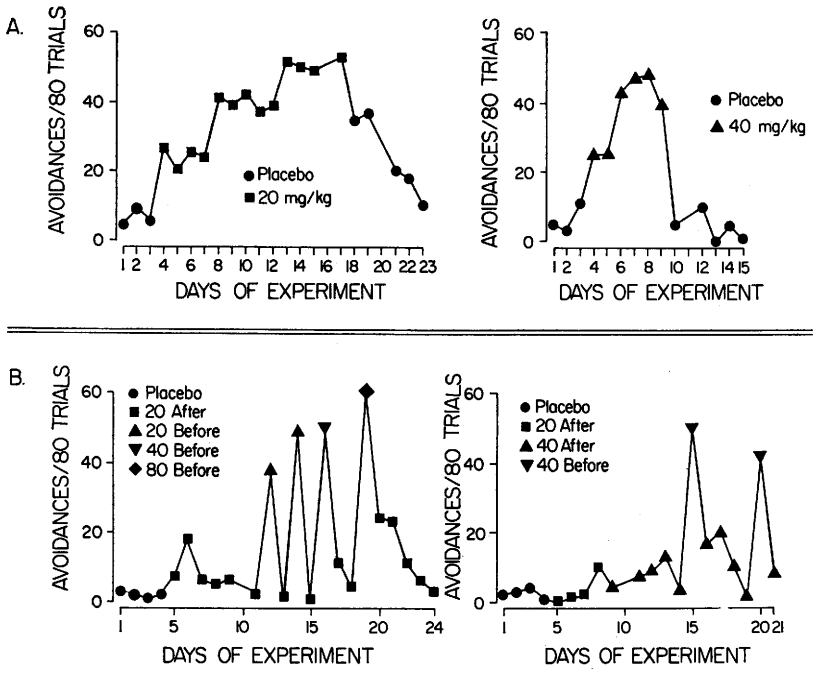

FIG. 1. Effect of marijuana on shuttle-box avoidance by poor performers. (A) Marijuana extract (20 or 40 mg/kg Δ^9-THC) was administered orally 2 hr before trials; four animals per group. (B) Marijuana extract (20, 40, or 80 mg/kg Δ^9-THC) was administered orally 5–15 min after or 2 hr before trials. Each graph represents a single rat.

irritation and peritoneal adhesions.

Results. Effect of marijuana on performance of trained rats. Figure 1a illustrates the effect of 20 and 40 mg/kg Δ^9-THC (as MED, given orally 2 hr before trials) on shuttle-box avoidance by animals designated as poor performers. They had undergone more than 800 trials prior to receiving drug. Performance was improved during the treatment period and dropped back to base line when MED was discontinued. Two additional trained animals were administered MED after trials for several days prior to receiving drug before trials. No significant performance change occurred during the period of treatment after trials but MED administered before trials produced a marked increase in avoidance responses (Fig. 1b). These results indicate that marijuana, like amphetamine, can improve avoidance performance of poorly performing rats.

Effect of marijuana on acquisition. Barrett and Leith (11) demonstrated that administration of amphetamine before each of a series of acquisition trials enhanced shuttle-box avoidance; however, the high avoidance levels were maintained only if amphetamine was withdrawn gradually. To examine the effect of marijuana on shuttle-box acquisition, 12 animals were divided into two equal groups; 6 rats received MED (20 mg/kg Δ^9-THC) before trials while the remainder served as controls. Marijuana markedly enhanced performance during the acquisition trials (Fig. 2a). The increased performance of the marijuana group as a whole reflects an increase in the percentage of animals with high performance levels. The avoidances per 80 trials on day 10 for each of the control animals were 1, 1, 1, 28, 54 and 76, while avoidances for the marijuana-treated animals were 29, 59, 63, 66, 69 and 72. Figure 2b illustrates that the performance of the marijuana group was maintained after the drug was discontinued. This is in contrast to the effect of marijuana on animals trained without drug, where avoidances were increased by MED but fell to predrug levels

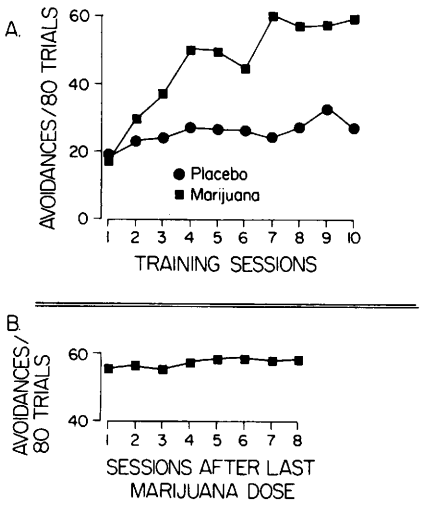

FIG. 2. Effect of marijuana on acquisition of shuttle-box avoidance. Each point represents the average from 6 rats. (A) Marijuana extract (20 mg/kg Δ^3-THC) was administered orally 2 hr before each training session. (B) Performance of marijuana group after discontinuation of drug.

when MED treatment was stopped. These results indicate that marijuana is similar to amphetamine with respect to the ability to facilitate acquisition of shuttle-box avoidance, but differs from amphetamine in that the performance levels of animals trained under marijuana are maintained upon abrupt discontinuation of the drug.

Discussion. Our finding that marijuana enhances acquisition of shuttle-box avoidance confirms the results of Park and Tilton (9). However, whether marijuana enhances or disrupts avoidance behavior seems to depend principally upon base line performance level rather than strain difference, although overall base line performance may vary in different strains. This is supported by our observation that MED decreases avoidances of trained, good performers but increases avoidances of trained, poor performers of the same strain. It is unlikely that the two effects are related to a single action of the drug since tolerance develops to the disruptive effect within 5–7 days while the facilitative effect increases with repeated administration.

Summary. Marijuana extract distillate enhanced shuttle-box avoidance of rats with a previously established base line of poor performance. When drug was discontinued, performance returned to base line. Marijuana facilitated acquisition of avoidance behavior; performance level was maintained after treatment ended. The data suggest that the facilitative effect is due to an action of the drug different than that which causes depression of conditioned behavior.

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