Physiological Psychology
1976, Vol. 4 (2), 155-158

The effects of a marijuana extract on two-choice discrimination learning in the squirrel monkey

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Eight adult male squirrel monkeys were given acquisition training on two-choice visual discrimination problems on form and color dimensions. Discrimination accuracy on both dimensions was impaired by .68 mg/kg of delta-9-tetrahydrocannabinol pretreatment. Response time was impaired on the first discrimination problem but evidence of tolerance development was present on the second. The accuracy impairment failed to show any evidence of tolerance development.

A number of studies have demonstrated the effects of marijuana and Δ^9-THC, generally considered the primary psychoactive component of marijuana, on the performance of a learned task. Marijuana has been found to impair the performance of a variety of operant schedules of reinforcement and included those requiring the subject to make a response contingent upon a spatial or temporal cue. This impairment has been demonstrated in pigeons (McMillan, Harris, Frankenheim, & Kennedy, 1970; Siegel, 1969), in rats (Boyd, Hutchinson, Gardner, & Merritt, 1963; Frankenheim, McMillan, & Harris, 1971), and in primates (Scheckel, Boff, Dahlen, & Smart, 1968).

Performance on tasks involving short-term memory was impaired by the acute effects of marijuana in subhuman primates (Ferraro, Lynch, & Grilly, 1972) and in man (Melges, Tinklenberg, Hollister, & Gillespie, 1970; Tinklenberg, Melges, Hollister, & Gillespie, 1970). Recent studies on the squirrel monkey have shown that the performance of a complex reinforcement schedule involving sequential responses was disrupted by the acute effects of a marijuana extract (Adams & Barratt, 1972, 1974).

Research on the effects of marijuana on the acquisition of new behaviors has been limited. Orsingher and Fulginiti (1970) found the effects of a marijuana extract impaired the learning of rats in a shuttlebox avoidance task as well as on the performance of a Lashley III maze.

The purpose of the present study was to determine the effects of a marijuana extract on the acquisition of a two-choice discrimination task involving either form or color cues. This research was designed to extend the earlier findings of an operant performance impairment to the acquisition of an operant response to the appropriate stimulus. The dependent measures included response accuracy and response time in order to differentiate the extent to which the impairment in acquisition was the result of a general motor deficit.

Results in this study were presented at the annual meeting of the Psychonomic Society, 1972. This research was supported by the Psychophysiology Program, Physiology Branch, Office of Naval Research, and by the Law Enforcement Assistance Administration, U.S. Department of Justice.

METHOD

Subjects

The subjects were eight adult male squirrel monkeys *(Samiri sciureus)* weighing between 600 and 700 g. The subjects were housed individually and fed a daily diet of fruit and commercially sold monkey chow, with ad lib access to a vitamin-supplemented water solution.

Apparatus

The apparatus consisted of a standard experimental cubicle (48 x 26 x 24 in.) with self-contained lighting, ventilation, and masking noise. The cubicle contained a stimulus panel consisting of two in-line projection units, each centered over a response lever (Lehigh Valley Electronics). The distance from the center of the stimulus unit to the respective lever was 2.5 cm. A drinking bottle was placed on one wall of the cubicle and was freely accessible throughout a session. A 94-mg sucrose pellet served as reward and was delivered through a Gerbrands feeder accompanied by a 1000-Hz tone for 1 sec. A six-pen event recorder marked the onset of the projected stimuli, the lever pressed, and the outcome (presence or absence of a reward) of each trial. Control of the stimulus display, reinforcement, response time recording, accuracy of choice behavior, and duration of the intertrial interval was done through programmed solid state and electromechanical equipment.

Procedure

The subjects were habituated to the restraining chairs for several weeks prior to the start of behavioral training. Following habituation, the subjects were placed in the cubicle and trained to press one of the two levers for food reward. During lever training, the subjects were given 100 trials per day (50 rewarded trials on each lever), with 30 sec between each trial. The intertrial interval was distinguished from the trials by the illumination of a 7-W lamp during the intertrial interval. During lever training, no cues were presented on the projection units. The response time was measured from the onset of a trial to the first response made on either lever. Lever training was continued until the subjects were responding equally on both levers as measured by their response time.

The subjects were divided into two groups and given either a marijuana extract (Marijuana Extract Distillate, NIMH)[1] at a dosage of .68 mg/kg of Δ^9-THC or a vehicle suspension of saline and Tween 80. All drug treatments were administered by intubation 60 min prior to the start of a daily session. During the acquisition of a two-choice discrimination problem, the positive stimulus occurred 50% of the time on the left and 50% on the right, with no side positive for more than four successive trials. The subjects were required to hit the correct side first in order to get rewarded, as a noncorrection procedure was used.

Table 1
Percentage Correct Responding During the Acquisition of Two-Choice Discrimination Problems as a Function of the Pretreatment With Δ^9-THC

Days	Triangle vs. Circle*	Green vs. Red*
	Saline-Tween 80 Treatment	
1	69 ± 2.9	59 ± 3.5
2	82 ± 2.7	68 ± 2.5
8	71 ± 2.2	64 ± 2.0
4	68 ± 1.9	76 ± 1.8
5	79 ± 1.5	85 ± 1.3
6	84 ± 1.4	84 ± 1.1
	Δ^9-THC (.68 mg/kg) Treatment	
1	56 ± 3.7	54 ± 4.0
2	53 ± 3.1	52 ± 4.0
3	58 ± 2.6	56 ± 2.0
4	50 ± 1.7	52 ± 3.8
5	52 ± 1.5	51 ± 1.0
6	55 ± 1.1	52 ± 1.0

**Means and the standard error are based on 100 trials per day.*

Table 2
Summary of Analysis of Variance on Form Discrimination Problem (Triangle vs. Circle) for Marijuana-Treated and Saline Controls

Source	SS	df	MS	F
Group	5334	1	5334	106.9*
Trials	602	5	120	12.9*
Group by Trials	582.5	5	116.5	12.6*
Error 1 (Uncorrelated)	299.2	6	49.8	
Error 2 (Correlated)	278	30	9.3	

**p < .001*

A procedure was used to impair the formation of a position habit. When eight successive responses were made to the same side, the positive stimulus was frozen on the opposite side until two consecutive correct responses occurred. This procedure was basically the same as that used by Glickstein, Barrow, and Luschei (1970).

In the first discrimination problem, a white triangle served as the positive stimulus and a white circle as the negative stimulus. Acquisition training consisted of 100 trials per day for 6 successive days (600 trials). A second discrimination problem consisted of a green disk as the positive stimulus and a red disk as the negative stimulus, with 100 trials per day for 6 days. Between the discrimination problems, the drug treatments were discontinued for 10 days and the subjects received daily sessions following the training format in order to insure response times on each lever were equivalent.

RESULTS

In the first discrimination problem, triangle vs. circle, the mean percentage of correct responses reached by the saline/Tween-80 group was significantly greater than for the marijuana-treated subjects. The marijuana-treated subjects failed to reach an 80% correct criterion within the 600 trials and failed to get above the 60% on any block of 100 trials, as shown in Table 1. The results of a repeated measures ANOVA indicated the differences between the saline/Tween-80 and marijuana-treated subjects were significant ($F = 106.9$, $df = 1/6$, $p < .001$). The trials effects were also significant, as was the Group by Trials interaction, as shown in Table 2.

On the second discrimination problem, green vs. red, the same effects under marijuana treatment were found on the accuracy of choice responses. As in the first problem, the saline/Tween-80 group reached a criterion of 80% correct responses, while the marijuana-treated subjects failed to make more than 60% correct responses for any daily block of 100 trials. The ANOVA results on the color dimension indicated the group differences were significant ($F = 94.00$, $df = 1/6$, $p < .001$). The trials and the Group by Trials interaction were significant, as shown in Table 3.

The response time data for the two treatment groups are given in Table 4. There was a significant difference between the two treatment groups in the mean response time for each of the daily sessions in the first discrimination problem. The saline/Tween-80 group responded significantly faster than the marijuana-treated subjects. A Kruskall-Wallis analysis of the response time data was significant ($H = 8.15$, $df = 1$, $p < .01$). However, in the second problem there were no significant differences between the group response times for the 600 trials.

A trial by trial analysis of the choice lever responding in relation to stimulus position and the outcome of the choice using Levine's method (1963 model) of determin-

Table 3
Summary of Analysis of Variance on Color Discrimination Problem (Green vs. Red) for Marijuana-Treated and Saline Controls

Source	SS	df	MS	F
Group	4525	1	4525	94.0*
Trials	798	5	160	14.5*
Group by Trials	1450.5	5	290	26.3*
Error 1 (Uncorrelated)	288	6	48.1	
Error 2 (Correlated)	330.8	30	11.0	

**p < .001*

Table 4
Mean Response Time During the Acquisition of Two-Choice Discrimination Problems as a Function of the Pretreatment With Δ^9-THC

Days	Triangle vs. Circle*	Green vs. Red*
	Saline Treatment	
1	1.60 ± .15	.94 ± .11
2	1.30 ± .12	1.19 ± .10
3	.95 ± .10	.88 ± .14
4	.95 ± .14	.93 ± .10
5	1.00 ± .12	.99 ± .12
6	.80 ± .11	.96 ± .14
	Δ^9-THC (.68 mg/kg) Treatment	
1	2.4 ± .09	.80 ± .03
2	1.8 ± .10	1.36 ± .09
3	1.9 ± .14	.85 ± .13
4	1.7 ± .11	.83 ± .12
5	1.4 ± .10	1.10 ± .15
6	1.3 ± .15	1.12 ± .16

**Means and the standard error are based on 100 trials per day.*

ing discrimination strategy indicated the saline-treated monkeys were using a strategy relating reward and stimulus position ($+I_S$ in Levine's terminology). In contrast, the marijuana-treated monkeys used either a response alternation (O_p) or position preference (I_p) hypothesis, both of which reduced the number of rewards the monkeys could obtain. The marijuana-treated subjects were found to use the position preference strategy early in the acquisition training and then switched to the position alternation strategy as training continued.

DISCUSSION

The results indicated that the marijuana-treated subjects were significantly impaired in the acquisition performance of both form and color discrimination problems as measured by the level of accuracy attained. In the form discrimination problem, there was a significant reduction in the speed at which the choice response was made. Motor impairment as measured by the response time deficits might, therefore, account for part of the inability of the marijuana-treated subjects to reach the criterion for acquisition. However, the trial by trial analysis of the hypotheses used to solve the discrimination problems indicated the marijuana-treated monkeys were not using a hypothesis compatible with criterion acquisition performance. In the second problem there was an acquisition performance impairment without a significant difference in response time. This would suggest that there was a learning deficit as well as possible performance impairment. The results of the statistical analysis indicated a significant Groups by Trials interaction which supports the conclusion that there was an acquisition deficit for the marijuana-treated subjects in both of the discriminations.

Examination of the acquisition data indicated the saline/Tween-80 group dropped in accuracy on the third session of Problem 1. This may have been the result of repeated vehicle treatment or a shift in problem solving strategy. The trial by trial analysis did indicate that the tendency for a position preference strategy found in the early sessions was overcome in the vehicle-treated group and was replaced by a strategy to repeat on the lever associated with the rewarded stimulus. The failure of the marijuana-treated subjects to improve in accuracy of choice selection was found to be due in part to a problem with position preference despite the correction procedure. The reduction in variability in the absence of improved accuracy across days on Problems 1 and 2 may be the result of the repeated administration of marijuana. The effect of repeated treatment may result in a more homogeneous response to the drug and thus produce less behavioral variability.

The results of the present study support evidence for an impairment in acquisition performance of both form and color discrimination problems as found earlier by Orsingher and Fulginiti (1970) in avoidance learning in rats. In the present study, there was an impairment on the color dimension, consistent with the findings of Siegel (1969) in pigeons, and on the form dimension. The broader range of impairment in the present study may be the result of species differences.

The nature of the present task required that the subject's short-term memory functioning be intact in order that the results of a response to the stimuli presented on the previous trial would be remembered. Data from other studies (Ferraro et al., 1972; Melges et al., 1970; Tinklenberg et al., 1970) have shown short-term memory in both lower primates and man to be disrupted by the acute administration of Δ^9-THC. The results of the present study are consistent with these findings, and it is suggested that an impairment in short-term memory function could account for the observed deficit in acquisition performance. The tendency of the marijuana-treated monkeys to use an hypothesis involving the position dimension rather than the stimulus cues may be due to an inability of these subjects to maintain continuity between the lever and its associated stimulus on a given trial. The 2.5-cm distance separating the stimulus image and the lever may have contributed to the difficulties of the marijuana-treated subjects in developing a stimulus-based hypothesis.

The results of the response time measure indicated the possible development of tolerance following repeated exposure to the effects of acute drug administration. There have been reports of tolerance developing to the effects of marijuana on learned behaviors (Black, Woods, & Domino, 1970; Carlini, 1968; Dewey, Harris, McMillan, Frankenheim, Turk, & Ford, Note 1; Ferraro & Grisham, 1972; Frankenheim et al., 1971; McMillan et al., 1970; Silva & Carlini, 1968). The evidence for tolerance development on unlearned tasks and on very complex behavioral situations has been inconclusive (Grilly, Ferraro, & Marriott, Note 2; Orsingher & Fulginiti, 1970; Thompson, Rosenkrantz, & Braude, 1971). It is suggested that tolerance to the behavioral impairment from acute intoxication with marijuana may be found on learned or established behavioral measures but that the effects on the acquisition of new behaviors and on more complex skills will not demonstrate tolerance unless there is the opportunity to compensate for the behavioral impairment, as suggested by Grilly et al. (Note 2) and Ferraro and Grilly (1973).

It is concluded that the acute effects of marijuana do produce a deficit in the ability of primates and subprimates to demonstrate acquisition of discriminations on both form and color dimensions. It is suggested that this deficit is partly the result of perceptual impairment, short-term memory impairment, and a general motor impairment which together impair the formation of a behavioral strategy appropriate for criterion performance.

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NOTE

1. The marijuana dosage levels were based on a concentration of 17.1% of Δ^9-THC in the marijuana extract distillate supplied by the National Institute of Mental Health which was diluted to a 40-mg/cc suspension in Tween 80 and saline.

(Received in Austin October 17, 1975.)