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Department of Pharmacology, University of Michigan, Ann Arbor, Michigan, and Laboratory of Psychobiology, Lafayette Clinic, Detroit, Michigan

Effects of Psychoactive Agents on Acquisition of Conditioned Pole Jumping in Rats*

By

EDWARD F. DOMINO, DONALD F. CALDWELL, and RACHEL HENKE

With 1 Figure in the Text

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Effects of psychoactive agents on operant behavior have been investigated for a variety of species (HERTZ 1960; SIDMAN 1959; BRADY 1958; and DEWS 1958). Evidence indicates the effect of these substances on conditioned avoidance behavior to be dependent on the organisms level of training at time of administration. Psychotomimetics such as LSD-25 and phencyclidine produce behavioral changes only in relatively larger doses for rats in contrast to those for man. Phencyclidine interferes with established conditioned avoidance in the rat only with doses which produce obvious disorganization of behavior (DOMINO 1964). It has been shown that morphine is much less effective than chlorpromazine in depressing conditioned avoidance behavior in dogs highly overlearned (DOMINO et al. 1963). Except in massive doses, l-hyoscyamine does not depress established conditioned pole jumping behavior (DOMINO and HUDSON 1959). On the other hand, much smaller doses of this drug cause a marked depression of the acquisition of the same behavioral response (MEYERS et al. 1964). Thus, it appears that there are at least two possible explanations: (1) that entirely different central neuronal mechanisms are utilized in the process of acquisition versus retention of conditioned behavior, or (2) that the neuronal mechanisms are the same but that certain drugs are more effective in interfering with the establishment of durable neuronal processes underlying memory.

The present study was designed to determine whether acquisition of an avoidance response in the rat is selectively affected by LSD-25 and phencyclidine. A sedative-hypnotic (amobarbital) was chosen to determine if these effects were limited to the psychotomimetics. Furthermore, a sympathomimetic agent (d-amphetamine) was included for investigation.

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Methods

The *S*s were 152 male, albino Sprague-Dawley rats 80—100 days old weighing 150—185 gms, housed in air conditioned quarters and maintained on an *ad libitum* food and water schedule. Three dose levels were studied for each of the four drugs (amobarbital sodium: 5, 10, 20 mg/kg; LSD-25: 25, 50, 100 μg/kg; phencyclidine: 200, 400, 600 μg/kg and d-amphetamine: 100, 500, 1000 μg/kg). All treatments were administered subcutaneously to groups of 10 rats and were given between 8:00 A. M. and 4:00 P. M. All drug dosages were as salt diluted in 0.9% saline. A control group received isotonic saline in an amount equivalent to four times the *S*'s weight in kilograms expressed in milliliters. This amount was equal to the largest volume received by the experimental *S*s. A second control group was not administered any injections. Testing began 25 min after injections at which time *S* was placed in the conditioned avoidance box for an additional 5 min of acclimatization before acquisition trials began. A 90 percent avoidance criterion was used. If criterion was not reached in 100 trials, the animals were eliminated from further testing.

The pole jump avoidance situation was a modification of the Cook and Weidley (1957) technique. The conditioned stimulus was a door buzzer sounding alone for 5 sec and then overlapping with a 5 sec 1 ma., 60 cps electric shock unconditioned stimulus. The pole was hung from the ceiling of the chamber to within 3 in. of the 36 sq. in. grid floor. The electric shock was passed through a Foringer grid shock scrambler. A 25 watt incandescent bulb provided light for the chamber at all times. The box was sound proof and contained a one way viewing glass. Randomized intertial intervals were employed with a mean time of 30 sec. Mean trials to a criterion of 9 out of 10 avoidance responses and mean total percent avoidance were compared for each drug group against performance of saline controls. Data were analyzed by analysis of variance and Student *t*-test techniques.

Results

Increasing amounts of both psychotomimetics (viz., LSD-25 and phencyclidine) caused a significant increase in mean trials to criterion for the middle and high drug doses, (see Fig. 1 and the Table). A corresponding decrease was observed for mean total percent learning; only the 25 μg/kg dose of LSD-25 did not differ significantly ($p < .20$) from the control group. Results for the sedative-hypnotic amobarbital produced a similar significant increase in mean trials to criterion for the 10 and 20 mg/kg doses. Analyses of mean total percent learning revealed a significant reduction only for the 20 mg/kg dose of amobarbital ($p < .01$). It should be noted that although increasing doses of LSD-25, phencyclidine, and

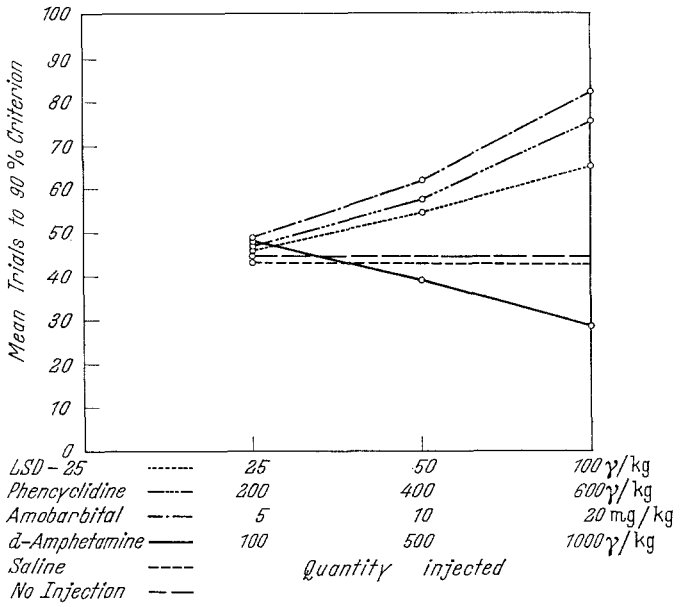

Fig. 1. Mean trials to 90 % avoidance conditioning criterion for rats administered either a psychotomimetic, sedative-hypnotic, or sympathomimetic drug. Each drug dose was administered to a separate group of rats

Table. *Mean trials to 90% response criterion and total percent avoidance behavior after various drug treatments with rats*

Drug	Dose	Mean trails and SD to 90 % avoidance criterion	Probability value attached to t-tests (comparison to saline)	Mean total percent avoidance ± 1 S.D.	Probability value attached to t-tests (comparison to saline)
LSD-25	25 μg/kg	45.7 ± 10.2	$p > .20$	41.2 ± 4.0	$p > .20$
	50 μg/kg	54.1 ± 6.4	$p < .02$	36.8 ± 4.2	$p < .01$
(N = 10/group)	100 μg/kg	64.1 ± 7.6	$p < .001$	33.9 ± 4.5	$p < .01$
Phencyclidine	200 μg/kg	47.7 ± 11.0	$p > .20$	38.2 ± 4.0	$p < .02$
	400 μg/kg	57.2 ± 14.8	$p < .05$	36.7 ± 5.4	$p < .01$
(N = 10/group)	600 μg/kg	76.6 ± 12.5	$p < .001$	31.5 ± 2.2	$p < .001$
Amobarbital	5 mg/kg	49.0 ± 7.9	$p < .20$	41.1 ± 5.0	$p > .20$
	10 mg/kg	60.2 ± 10.0	$p < .01$	43.4 ± 4.3	$p > .20$
(N = 10/group)	20 mg/kg	81.7 ± 14.1	$p < .001$	34.2 ± 6.9	$p < .01$
d-Amphetamine	100 μg/kg	48.1 ± 8.5	$p > .20$	43.3 ± 7.3	$p > .20$
	500 μg/kg	38.5 ± 9.7	$p < .10$	47.7 ± 5.9	$p < .20$
(N = 10/group)	1000 μg/kg	27.4 ± 10.0	$p < .01$	48.8 ± 6.3	$p < .10$
0.9 % Saline N = 22		43.1 ± 17.5		44.2 ± 8.4	
No injection N = 10		44.6 ± 11.8	$p > .20$	41.6 ± 3.4	$p > .20$

amobarbital have similar effects on mean trials to criterion, they differed in their effects on the variances. Whereas the standard deviation increased with increasing amounts of phencyclidine and amobarbital, the reverse was noted for LSD-25. An opposite dose-response relationship was observed for mean trials to criterion for d-amphetamine when compared to the psychotomimetic and sedative-hypnotic drugs. Although significance was reached only for the 1 mg/kg dose ($p < .01$), increasing amounts of this substance decreased trials to criterion in a linear manner. Variance increased with dosage. The effect of increasing dosage on mean percent avoidance was not marked as for the psychotomimetic and sedative-hypnotic drugs (see Table). No differences were observed between saline treated and no injection control groups confirming the validity of saline as a control substance for this task.

Discussion

The data clearly indicate that for all doses of LSD-25, phencyclidine, and amobarbital studied rate of acquisition of a conditioned avoidance response is reduced, although only significantly for the higher doses. Furthermore, this effect occurred with doses of these agents demonstrated to show no significant effect on conditioning in overtrained animals performing essentially the same task (Cook and Weidly 1959; Domino 1964). The effect for the psychotomimetics appears to be nonspecific as evidenced by the similar action of amobarbital, a sedative-hypnotic agent in reducing rate of acquisition of avoidance learning. For the small doses of psychotomimetics used in this study, negligible changes in gross overt behavoir were noted. This is in contrast to the gross behavioral deficits observed for doses of amobarbital administered. It would be of considerable theoretical interest to show that the psychotomimetic agents selectively affect certain conditioned responses depending upon the sensory modality used. Thus, on the basis of data currently in the literature one might expect LSD-25 to affect a visually oriented task more than one predominently auditory in nature; phencyclidine might affect more selectively tasks involving proprioceptive cues. Nevertheless, it is of interest that behavior depending on an auditory conditioned stimulus is affected by all the drugs utilized in this investigation. This poses the question whether auditory input is exclusively affected or whether these drugs also exert actions on other functions of the brain such as association processes, memory, motivation, and/or motor function. Further investigation of this point is clearly indicated.

Although both d-amphetamine and LSD-25 share some sympathomimetic actions, their effects on acquisition are clearly different. d-Amphetamine caused a slight facilitation of acquisition, but this was significant ($p < .01$) only at the 1.0 mg/kg dose.

Summary

Albino rats required progressively more trials to reach a 90 percent avoidance criterion and achieved less mean total percent avoidance learning than saline injected controls following administration of increasing doses of LSD-25, phencyclidine and amobarbital. The psychotomimetics were effective in depressing acquisition in dosages demonstrated by others to be ineffective in overtrained animals. In contrast d-amphetamine had a slight facilitating effect, but only in large doses.

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Dr. EDWARD F. DOMINO,
Dept. of Pharmacology, University of Michigan, College of Medicine, Ann Arbor, Michigan, U.S.A.