Effects of agroclavine on avoidance behavior in the hamster

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Four groups of hamsters received 0, 2, 6, or 10 mg/kg of agroclavine. The two highest dosage levels severely retarded avoidance learning, whereas the 2 mg/kg group showed no decrement in learning. Gnawing was prevalent in the 6 and 10 mg/kg groups.

Whereas LSD-25 has been the object of considerable behavioral research, little experimentation has been done on related hallucinogens. Both elymoclavine and agroclavine have chemical structures quite similar to LSD: They also appear to cause some similar behavioral effects, e.g., hyperirritability, mydriasis, Straub tail effect (Rothlin, 1957).

Low doses of LSD improved avoidance performance in rats (e.g., Jarrard, 1963; Hamilton, 1960), whereas large doses of LSD impaired such behavior (e.g., Jarrard, 1963). A similar nonmonotonic relationship was found for the effects of elymoclavine on general activity in mice (Harsh & Witters, 1970). Ray & Wong (1967) reported that avoidance learning was facilitated by low and medium doses of elymoclavine. No impairment of learning was found at their highest dose level (300 mg/kg).

The present experiment was designed to investigate the relationship of agroclavine to avoidance learning in the hamster.

METHOD

Subjects and Apparatus

The Ss consisted of 46 naive random-bred golden hamsters (Engle Laboratory) with weights ranging from 80 to 123 g. There were 16 male and 30 female hamsters.[1] They were caged individually and maintained on ad lib food and water.

The apparatus has been described previously by Melvin, Athey, & Heasley (1965). It is made up of a 1-ft startbox, a 4-ft straight alley, and a wide black goalbox. The alley and the startbox were painted white and had glass lids and grid floors. The startbox was divided into upper and lower compartments by a trapdoor, hinged on one side and suspended 6 in. above the grid floor. The S was prevented from leaving the upper compartment by a barrier. Reentering the alley was prevented by a manually operated guillotine door at the entrance to the goalbox.

Response times were recorded to 0.01 sec by photocells and associated electronic equipment. Alley time was defined as the time elapsing from the interruption of a beam of light 12.5 in. from the rear of the startbox until the interruption of a beam 0.5 in. inside the goalbox. Total time was defined as the time from release of the trapdoor to the interruption of the goalbox photobeam. Voltage was delivered by way of a 10K ohm series resistor and monitored by a vacuum-tube ac voltmeter. On all shock trials, shock intensity was 55 V ac. A white noise generator provided masking noise for the duration of all trials.

Procedure

Three groups of Ss were given a 2-, 6-, or 10-mg/kg dose of agroclavine dissolved in a 0.5% solution of sodium tartarate in distilled water. Agroclavine concentrations were adjusted so that each animal received a volume of approximately 0.5 ml. Controls (Group 0) were injected with the solvent alone. A 5-min period was spent in a waiting cage after the injection in order to give time for the drug to take effect.

The hamsters were randomly assigned to four groups of 10 Ss each.[2] Each S was placed in the goalbox for a 10-min exploration period with the door open. Following the exploration period, each S was then injected intraperitoneally. Following the injection procedure, each hamster was placed on the trapdoor facing the goalbox and dropped into the startbox several times to acquaint S with this routine. The hamster was allowed to proceed to the goalbox with the shock off. This phase was 10 min in duration. All Ss then received identical avoidance training, with a shock in the startbox and alley being initiated 5 sec after release of the trapdoor. When the hamster entered the goalbox, the door was lowered and S remained there for a 30-sec period. If the animal entered the goalbox within 5 sec, it experienced no shock. The acquisition criterion was 5 consecutive avoidance trials within a 40-trial limit.

RESULTS

The effects of agroclavine on the number of trials to meet the avoidance criterion are shown in Fig. 1. A Kruskal-Wallis one-way analysis of variance found these differences significant ($H = 16.52$, $p < .001$). As the figure indicated, however, agroclavine interferes with learning only at the two highest dose levels. Mann-Whitney U tests revealed that Group 2, while not significantly different from Group 0, showed quicker learning than either Group 6 ($U = 9$, $p < .002$), or Group 10 ($U = 9$, $p < .002$). The control group, Group 0, also learned faster than either Group 6 ($U = 0$,

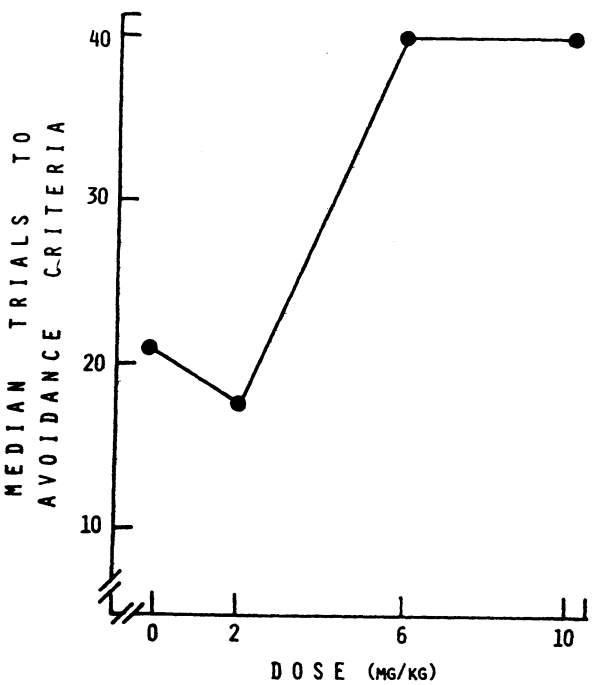

Fig. 1. Median number of trials to learn the avoidance response as a function of agroclavine dose level.

$p < .002$), or Group 10 ($U = 13$, $p < .02$).

The number of animals in each group which reached the avoidance criterion within 40 trials is as follows: Group 0 ($N = 8$); Group 2 ($N = 8$); Group 6 ($N = 1$); and Group 10 ($N = 1$). A comparison of Groups 0 and 2 vs Groups 6 and 10 revealed significance (chi square = 20.70, $p < .001$).

At times, treated hamsters were observed to gnaw the apparatus, a response which competed with successful avoidance. The number of hamsters per group which gnawed at any time in the apparatus was as follows: Group 0 ($N = 0$); Group 2 ($N = 4$); Group 6 ($N = 9$); and Group 10 ($N = 7$). These differences were significant (chi square = 18.40, $p < .001$).

DISCUSSION

These results indicate that high dose levels of agroclavine retard or prevent the learning of avoidance in hamsters. The low dose level did not retard performance. Indeed, the 2-mg/kg dose group learned in slightly fewer trials than the control group. Although this difference was not statistically significant, it is in the direction found by other investigators with LSD in rats (e.g., Jarrard, 1963), and elymoclavine in mice (Ray & Wong, 1967). Unlike the latter study, however, high dose levels of agroclavine interfered with avoidance.

Harsh & Witters (1970) reported that elymoclavine increased activity (wheel-running) at low dosages and decreased it with high dosages. This may have been the case in the present study, however the frequency of gnawing increased at high dose levels. Since gnawing is incompatible with running, this behavior was obviously a factor in the lack of learning shown by Groups 6 and 10.

Our control-group hamsters showed reasonably good one-way avoidance learning with this running response. The effect contrasts with the results of Babbini & Davis (1967), who obtained only 9.48% avoidance responses. Our Group 0 avoided on 42.12% of the trials. Thus, the straight runway appears to be a more suitable apparatus for one-way avoidance in hamsters than the four-compartment box used by Babbini and Davis.

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NOTES

1. Through a procedural error, the groups varied in terms of sex ratio. However, analysis revealed that sex of S had no substantial or significant effects on performance.

2. A fifth dosage level (24 mg/kg) was administered to six hamsters. Since none of these Ss learned the avoidance task and two Ss died within 1 h of injection, this dose level was discontinued.

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