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The Effect of LSD-25 on Spatial and Stimulus Perseverative Tendencies in Rats*

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Introduction

WERNER, WAPNER, KRUS and their associates (e.g., 1959) have suggested that the administration of LSD-25 results in a "regression" to more primitive states; and further, that there are "formal similarities" between the cognitive-perceptual processes of organisms under LSD-25 intoxication and the mental processes of young children, schizophrenics, and brain-injured *Ss*. One of the postulated "regressions" with direct relevance for learning situations is that of "rigidity". For example, WERNER (1948) postulates that primitive organisms lack the flexibility to manipulate their surroundings and therefore respond in a fixed invariable manner to their environment.

Consistent with this developmental interpretation of the action of LSD-25 are the findings of PAWLOWSKI (1962) which indicate that LSD-25 results in an increase in perseverative tendencies (rigidity) in rats. These rats continued to make a jumping response which they had previously learned even though the situation required a modification of the jumping response. Similarly, WILPIZESKI and HAMILTON (1964) report that rats receiving a 0.5 mg/kg dosage of LSD-25 were unable to inhibit a previously-correct position response during spatial reversal learning. However, the question may be asked whether the perseveration noted by PAWLOWSKI and by WILPIZESKI and HAMILTON results from a general perseverative tendency or from some artifact specific to the experimental situations. To assess the various types of perseveration produced by LSD-25 two studies were performed: the first study evaluates the influence of LSD-25 on *spatial* perseverative tendencies; the second study involves the effect of LSD-25 upon *stimulus* perseverative tendencies.

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Experiment I

Procedures

Subjects. One hundred and twenty-eight albino rats weighing approximately 230gms. were employed in the investigation.

Apparatus. A maze consisting of a starting box ($9\frac{1}{2}'' \times 6'' \times 12''$), a runway ($12\frac{1}{2}'' \times 6'' \times 12''$), a choice point ($14\frac{1}{2}'' \times 11'' \times 12''$) with two vertically swinging doors ($5'' \times 4''$) and two goal boxes ($14\frac{1}{2}'' \times 6'' \times 12''$) was utilized. A panelescent light was mounted on the back of both doors. Except for the preliminary training session, one panelescent was always off and the other set at 117 volts.

The floor of the starting box, runway, and choice point consisted of a brass electric grid.

Preliminary Training. The first 40 trials during the initial experimental session consisted of preliminary training in opening the plexiglass doors leading to the goal boxes. The animals were forced to the right goal box on 20 trials and to the left goal box on 20 trials. If the animal did not enter a goal box within 10 sec the grid was electrified. When the animal entered the goal box, the shock was terminated and the animal was removed from the maze. Since there were marked individual differences in tolerance to shock, during the first 10 trials the investigator established an appropriate shock level for each rat, one which elicited rapid running without squealing or attemps to jump out of the apparatus.

Preference Measurement. The last 20 trials of the first experimental session were utilized to measure the strength of the animal's position and brightness preferences. Both doors, one of which was bright (117 volts) and the other dark (0 volts), were exposed simultaneously and passage through both doors was unimpeded. The right-left placement of the bright stimulus was randomized.

Half of the 128 animals revealed strong position preferences (at least 18 out of 20 trials to either the right or left door). The 64 animals that did not manifest strong position preferences were required to learn (to a criterion of at least 18 errorless trials out of 20) a right-left position discrimination at the beginning of the second experimental session. The door leading to the incorrect goal box was locked from behind. A correction procedure was employed throughout the remainder of the experiment.

Brightness Training. All animals were switched from their position preferences to a brightness discrimination in which the bright door was correct for half the animals and the dark door was correct for the other half. The right-left placement of the bright stimulus was randomized. Brightness training continued for two 50-trial training sessions spaced a week apart or until the animals reached a criterion of 18 errorless trials out of 20.

Eight minutes before the beginning of brightness training half the animals were given i. p. a 0.5 mg/kg dosage of lysergic acid diethylamide. The remaining 64 animals served as placebo controls receiving i. p. a 5 cc/kg dosage of distilled water.

For the placebo animals, the same shock level utilized during preliminary training and preference measurement was employed during brightness learning. Since LSD-25 produced a marked increase in sensitivity to shock (due to an increase in salivation and consequent soaking of the ventral hair), the shock level for the LSD-25 animals was reduced during brightness training to one-third of the voltage employed in the earlier experimental sessions. (Pilot studies had indicated that for wet rats one-third the normal voltage was equivalent to the full voltage used for dry rats, as measured by number of trials to learn a brightness discrimination and speed of running in the maze.)

Results

Position Perseveration Scores. A position perseveration score was derived for each animal by subtracting the number of error trials to the *non-preferred* side from the number of error trials to the *preferred* side during brightness discrimination learning.

Table 1. *Mean perseveration scores (position and stimulus) and trials-to-criterion for LSD-25 and placebo Ss in experiments I an II*

Experiment I

Drug groups	Position perseveration scores	Trials to criterion
LSD-25	7.46	65.63
Placebo	2.98	53.59

Experiment II

Drug groups	Stimulus perseveration score	Trials to Criterion
LSD-25	2.83	26.11
Placebo	5.50	32.78

Table 2. *Distribution of position perseverative streaks for LSD-25 and placebo Ss in experiment I*

Drug groups	Number of position perseveration streaks		
	0	1–2	3–7
LSD-25	26	27	11
Placebo	46	16	2

Analysis of the position perseveration scores indicated that the LSD-25 animals made significantly ($p < .001$) greater scores than did the placebo animals. Table 1 shows the mean position perseveration scores for the two drug groups.

Trials to Criterion. A significant ($p < .005$) difference appeared between the mean trials scores of the two drug groups. Table 1 shows that the LSD-25 animals required more trials to learn the brightness discrimination than did the placebo animals.

Position Perseverative Streaks. In addition to the position perseveration scores, it was anticipated that position rigidity would manifest itself in the form of continuous streaks of running to the preferred side. Each

time an animal ran nine or more times (within each block of ten trials) to its preferred position, it was credited with one position perseverative streak.

Chi square analysis yielded a significant difference ($p < .01$) between the LSD-25 and placebo groups. As indicated in Table 2, 11 LSD-25 compared to only two placebo animals compiled between three and seven streaks while only 27 LSD-25 animals compared to 46 placebo animals failed to compile any streaks.

Experiment II

Procedures

Subjects. Thirty-six albino rats were utilized.

The identical *apparatus*, *preliminary training*, and *preference measurements* utilized in the first study were employed in the second study. All 38 rats manifested strong initial spatial preferences (at least 18 out of 20 trials to one side) for the right position.

Brightness Training. During the second experimental session, all animals were first trained to respond to the bright door (117 volts) and to avoid the dark door (0 Volts). On half the trials, the bright door was on the right, on the other half, on the left. Training was continued until the animals reached a criterion of 18 errorless trials out of 20.

Position Training. Immediately following the completion of brightness training, the animals were switched to a position discrimination problem in which the brightness value of the doors was an irrelevant cue. Half the animals were trained to respond to the right door, the other half to the left door. The right-left placement of the bright stimulus was randomized. Training was continued until the animals reached a criterion of 18 errorless trials out of 20.

Eight minutes before the beginning of position discrimination training, half the animals received an i. p. injection of LSD-25 (0.5 mg/kg). The other half received i. p. injections of distilled water (5 cc/kg). The LSD-25 and placebo groups were matched for number trials required to learn the brightness discrimination.

As in the first study, for the placebo animals the same shock level utilized during preliminary training and preference measurement was employed during position discrimination training, while for the LSD-25 group the shock level was reduced the one-third of the voltage employed in the earlier experimental sessions.

Results

Stimulus Perseveration Scores. A stimulus perseveration score was computed for each rat by subtracting the number of error trials to the dark door from the number of error trials to the bright door during the learning of the position discrimination.

As indicated in Table 1, the placebo animals made statistically significant ($p < .025$) *higher* stimulus perseveration scores than did the LSD-25 animals.

Trials to Criterion. Table 1 shows that the LSD-25 group required significantly ($p < .05$) *less* trials to learn the position discrimination than did the placebo group.

Stimulus Perseverative Streaks. Every time an animal ran nine or more times (within a block of ten trials) to the bright stimulus, it was credited with one stimulus perseverative streak.

No significant results appeared in the analysis of the stimulus perseverative streaks. However, the distributional trend shows that the placebo animals (eight streaks) manifested more stimulus perseverative streaks than did the LSD-25 animals (four streaks).

Discussion

Taken together, the results of the two studies at first appear opposed. In the first study, the LSD-25 animals revealed marked position perseveration and required a large number of trials to shift from a position to a brightness discrimination. In the second study, the LSD-25 group manifested relatively little stimulus perseveration and learned to shift to a position discrimination more quickly than did the placebo controls. The results may be reconciled, however, by observing that in both studies the LSD-25 rats are perseverating a position response tendency or set. In the first study, since the animals obtained reinforcement for responses to the brightness dimension, perseveration of a position response tendency resulted in more errors; in the second study, since the animals received rewards for position responding, perseveration of a position set resulted in fewer errors and more rapid learning by the LSD-25 group.

These findings have direct implications for hypotheses concerning the nature of perseverative response tendencies. It was anticipated originally that whatever response tendency was dominant at the time of LSD-25 injection would become rigid and invariable. Based upon the assumption of perseveration of the momentarily dominant response tendency, position perseveration was anticipated in the first study, stimulus perseveration in the second study. However, the dominance of position responding in both studies suggests that the response set manifested under LSD-25 is not necessarily the momentarily dominant one, rather the one that is most natural or initial (i.e., the member of a hierarchy of response tendencies most easily elicited) in a particular testing situation. During the preliminary preference testing in both studies, most rats manifested strong position response tendencies. In Experiment I, 64 rats showed strong initial position preferences (at least 18 out of 20 preference trials to one position) and an additional 32 animals revealed some pref-

erence for one position (between 11 and 17 out of 20 preference trials to one position). In Experiement II, all 36 rats used showed strong position preferences. Thus, in both experiments the initial tendency of the rats was to respond on the basis of position and the effect of LSD-25 was to produce a perseveration of their initial position tendencies.

In addition to their importance for perseveration concepts, the present results also may have pertinent physiological implications. Some recent investigations have suggested that stimulus and position perseverative tendencies may be related to different neuroanatomical structures. MISHKIN (1964) reports that stimulus perseveration is produced by ablation of the orbital frontal cortex while position perseveration appears to involve the dorsal-lateral frontal cortex. BITTERMAN (1965) reports that extensive cortical lesions in the rat produce retardation on the reversal of visual discriminations (stimulus perseveration) but no deficit on position reversals (position perseveration). The possibility that LSD-25 is effecting differentially neural structures involved with the inhibition of position and stimulus response tendencies suggests the utility of investigations concerned with the relationship between adaptive behavior and the localized application of LSD-25 to different brain structures.

Besides their implications for perseveration and physiological concepts, the present findings suggest a shift of emphasis in psychopharmacological learning studies. Typically, the drug investigator concerns himself with the correlation between drug administration and the learning and/or retention of a simple learning task (e. g., rope climbing, bar pressing). The results of the present studies suggest that analyses involving simple performances may sometimes be misleading. The ambiguity in the seemingly opposed results of the two studies was resolved by transcending the simple performance scores through an analysis of the animals' response tendencies. The critical question is not whether LSD-25 impairs or accelerates learning, rather how does LSD-25 influence the organism's characteristic ways of coping with its environment. In the first study, LSD-25 impaired speed of learning; in the second study, LSD-25 accelerated speed of learning-but in *both* studies, the administration of LSD-25 resulted in a fixation of a single mode or means of environmental adjustment (perseveration of position response tendencies).

Summary

Two studies were performed to investigate the effect of LSD-25 on position and stimulus perseverative tendencies in rats. In Experiment I, rats with strong position habits learned a brightness discrimination (in which position was an irrelevant cue) after LSD-25 or placebo injections. The LSD-25 animals showed more position perseveration and slower

learning than did the placebo controls. In Experiment II, rats with brightness preferences learned a position discrimination (in which brightness cues were irrelevant) under LSD-25 or control conditions. Compared to the placebo animals, the LSD-25 rats manifested less stimulus (brightness) perseveration and learned the position discrimination more quickly.

The results of the two eperiments indicate that LSD-25 does not procedure a perseveration of any momentarily dominant response tendency, rather a perseveration of the animal's most natural or initial response tendency in the particular experimental situation.

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