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Effects of Lysergic Acid Diethylamide on Simple Instrumental Conditioning, Extinction and Discrimination Learning in the Rat[1]

ALEXANDER J. ROSEN AND JOSEPH A. BUGA

University of Illinois at Chicago Circle, Chicago, Illinois 60680

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ROSEN, A. J. AND J. A. BUGA. *Effects of lysergic acid diethylamide on simple instrumental conditioning, extinction and discrimination learning in the rat.* PHARMAC. BIOCHEM. BEHAV. 1(6) 619–627, 1973. Hungry rats were trained under placebo or LSD (high and low dose) conditions to either run in a straight alley for food or lever press (FR20) in a Skinner box in the presence of one of two spatially positioned bars associated with food reward. A testing phase followed in which animals continued to perform under either the same injection conditions or under one of the alternative injection conditions. The results indicated that high drug doses (0.20 mg/kg) increased resistance to extinction in the runway but impaired both running acquisition and discrimination whereas low doses (0.05 mg/kg) impaired running but improved discrimination. There were some indications that LSD had long-term behavioral consequences which outlasted the drugged state, suggesting an effect on learning as well as on performance.

LSD Instrumental conditioning Discrimination learning Extinction

CLINICAL tests have reported that subjects given LSD (d-lysergic acid diethylamide) in psychotherapeutic settings learned a variety of concepts while under the influence of the drug and that the ensuing behavioral changes outlasted the drugged state. [8]. These data however, which derive largely from uncontrolled observations, are at variance with a large body of literature concerned with the effects of LSD on lower animals which suggests that the effects of the drug are largely transitory in nature and are related to performance variables such as attention and motivation rather than to long-term learning variables [1].

Many attempts to explain the behavioral effects of LSD have focused on what Key [14] has described as the level of significance of sensory stimuli. LSD is presumed to change the level of responsiveness to environmental events and thus alter the meaning of the sensory input. A biphasic effect of the drug is suggested with low doses increasing stimulus significance and high doses producing distraction. Biphasic dosage results have in fact been reported in a variety of discrimination tasks [1]. A similar explanation of the drug's behavioral effects has been offered by Bignami [5] who suggested that LSD affects the meaning of the stimuli that the organism has experienced in the past. Within this theoretical context, the behavior seen after LSD administration would be related to concurrent perceptual or motivational distortions that may facilitate or impair performance. These behavioral changes however would be confined to the presence of the drug and should not outlast its immediate CNS influences, whether direct or indirect. The effects of the drug therefore would be relegated to performance variables having to do with perception, motivaiton, or inhibition rather than learning.

The present investigation provides a test of the hypothesis that LSD effects learning and/or performance by utilizing a factorial design procedure [16]. Previous investigations [1] have typically used animals that were already trained in a discrimination task before drug injections were administered. Therefore, none of the reported effects can be specifically tied to a modulation of the learning process itself since changes in behavior such as those reported may derive from interference with performance variables. In a factorial design, animals are trained under either placebo or drug conditions selected to produce different performance levels and then are tested under the same or switched injection conditions. If long term consequences or residual effects of the training variables, as indexed by slow behav-

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ioral adjustments to changed injection conditions in testing, are obtained, then effects on learning are suggested. Effects on performance are reflected in relatively abrupt behavioral adjustments to the changed injection conditions, indicating no residual effect of the previous training conditions. In the context of avoidance conditioning Banerjee [3] has in fact hypothesized that LSD may have different effects on learning and performance.

The specific parameters used in the present study derive from previous reports. Investigations dealing with behavior maintained by intermittent reinforcement schedules have shown that ip doses of LSD between 0.04 mg/kg and 0.50 mg/kg produced decreases in operant performance and periodic interruptions of responding in the rat [1]. Disruptions in responding have been noted between 5 and 10 min after injection [2] and peak effects occurred within 30 min after injection regardless of dose level [8]. The effects of the drug were found to persist for approximately 90 min after injection [12]. Most of the studies that have investigated the behavioral effects of the drug over a wide range of doses have shown the resultant dose-response curve to be a decreasing negatively accelerated function [2,10]. Jarrard [13] has suggested that LSD may have dose-dependent biphasic effects on behavior.

EXPERIMENT 1

METHOD

Animals

Forty-five naive male albino rats, approximately 90 days old upon arrival from Holtzman Co., Madison, Wisc. were used.

Apparatus

Two Lehigh Valley test cages (Model 1316) with sound attenuating hulls (Model 1316C) were used. Each cage contained two retractable levers (Model 123-05) and a pellet dispenser that provided food reinforcement (0.045 g Noyes pellets). A nonretractable lever (LVE Model 121-05) was added to the test cage for pretraining. Programming of contingencies was accomplished with BRS solid state module circuitry. Presin (Model C-3 Moduprint) printout counters were used for recording of dependent variables.

Procedure

Animals were housed in individual cages and placed on a 23 hr food deprivation schedule with water available ad lib. They were given one hour of free access to Purina Lab Chow 90 min after the completion of an experimental session to control for the possibility of residual drug effects depressing food consumption. Pretraining began after 3 days of magazine training. The animals were trained for a period of three weeks at the same time of day, to press a lever that was centered on the wall opposite to, and the same height as, the retractable levers, and the ratio of responses necessary for reinforcement was gradually raised to FR 20. During this phase the two levers that were later used for discrimination training were retracted.

Animals were then divided into 3 groups equated for body weight and FR 20 rate at the end of the pretraining phase. The first group of 15 rats received IP injections of isotonic saline equal in volume to the highest drug dosage given other animals. The second group of 15 animals received IP injections of 0.05 mg/kg LSD in saline solution (0.10 mg/cc), and the third group received 0.20 mg/kg LSD IP. Injection days were always separated by 72 hr. LSD solutions were prepared from the tartrate salt in saline and were kept frozen in sealed 30 cc vials when not in use.

Twenty-five min after injection the animal was placed into the test apparatus and after 120 sec either the left or right bar was presented. For half of the animals in each group the left bar was positive (S+). Completion of a FR 20 on this bar led to a 10 pellet reward and the trial ended, followed by an intertrial interval of 120 sec with house light off and both bars retracted. Bar pressing on the right bar, when it was presented, was not reinforced for these animals and a negative trial ended after either 20 bar presses or 30 sec. The positive and negative stimuli were reversed for half the animals in each group. All animals received 10 trials per session with the left and right levers presented 5 times each in a predetermined random order that was changed daily. Sessions always began with a presentation of the positive stimulus and no more than 2 positive or 2 negative stimulus presentations occurred consecutively. This training phase continued until all animals completed 5 sessions (50 trials, 25 to S+ and 25 to S).

During the testing phase each group was split into 3 subgroups that were equated for body weight and FR 20 rate on both positive and negative bars during the last 20 trials of training. An additional 50 trials were run in which one subgroup continued at the training phase injection condition and the other 2 subgroups were switched to the alternative injection conditions. Thus in the testing phase 9 groups were formed determined by the factorial combination of training and testing injection conditions: (1) SAL-SAL; (2) SAL-LSD.05; (3) SAL-LSD.20; (4) LSD.05-SAL; (5) LSD.05-LSD.05; (6) LSD.05-LSD.20; (7) LSD.20-SAL; (8) LSD.20-LSD.05; (9) LSD.20-LSD.20. The dependent variable was response latency, recorded to the nearest tenth of a second, from the insertion of the lever to the first bar press.

RESULTS

Response latencies were reciprocalized, converted to speed scores, and subjected to mixed design analyses of variance [17] with injection conditions as the between animals sources of variance and trial blocks as the within animals source of variance. For each pair of trials a differential response speed, defined as the difference between response speed on the positive and negative bar (DRS = R(S+) R(S)), was calculated and these data were used in the analyses and are presented graphically in Fig. 1. The use of the DRS measure reflects the discriminatory behavior of the animals more clearly than separate consideration of the positive and negative bar data although analyses of these separate data were performed and will be discussed where appropriate.

Training

All groups improved over trials with the low dosage animals responding faster than subjects in the other two groups toward the end of training. The analysis revealed a significant trial blocks effect ($F = 35.37$, $df = 4,144$, $p<0.01$) and a significant groups x trial blocks interaction ($F = 2.25$, $df = 8,144$, $p<0.05$). Further analysis revealed that the low dose group was superior to the other two groups on trial blocks four and five ($F = 11.26$, $df = 1,144$,

$p<0.01$). This difference in DRS resulted from superior positive bar responding by the low dose subjects ($F = 38.18$, $df = 1,144$, $p<0.01$) on the last two trial blocks. There were no differences between the groups on negative bar performance. Additional analyses revealed that there were no differences within each of the groups (n = 15) when each group was considered as comprised of three independent subgroups (n = 5) that received different testing treatments.

Testing

There were clear indications of both training and testing effects as well as interactions in the overall data (Fig. 1) and the analyses of these data were broken down into specific predetermined comparisons of interest. The first comparison considered only those groups whose injection condition remained unchanged (SAL-SAL; LSD.05-LSD.05; and LSD.20-LSD.20). The second comparison (SAL vs LSD.05) included only those groups that received either saline or the low LSD dose (SAL-SAL; LSD.05; LSD.05-LSD.05; and LSD.05-SAL). The third comparison (SAL vs LSD.20) included only those groups that received either saline or the high LSD dose (SAL-SAL; SAL-LSD.20; LSD.20-LSD.20; and LSD.20-SAL). The final comparison (LSD.05 vs LSD.20) considered only those groups that received high or low LSD doses throughout (LSD.05-LSD.05; LSD.05-LSD.20; LSD.20-LSD.20; and LSD.20-LSD.05).

Analysis of the three unswitched groups (SAL-SAL, LSD.05-LSD.05, and LSD.20-LSD.20) revealed a clear biphasic effect of the drug. Injections of 0.20 mg/kg caused significantly lower DRS scores than placebo injections ($F = 4.86$, $df = 1,16$, $p<0.05$), whereas 0.05 mg/kg injections resulted in significantly higher DRS scores than placebo ($F = 8.33$, $df = 1,16$ $p<0.05$) over the five blocks of test trials.

SAL vs LSD.05

The DRS exhibited by the LSD.05-LSD.05 group was significantly larger than that of the other 3 groups ($F = 13.41$, $df = 1,16$, $p<0.01$) which did not differ from each other. There was a significant effect for the 0.05 mg/kg LSD injection during training ($F = 4.94$, $df = 1,16$, $p<0.05$) and the training by testing interaction was significant ($F = 6.03$, $df = 1,16$, $p<0.05$). The significant results in this analysis were caused by the large DRSs exhibited by the LSD.05-LSD.05 group. These findings were reflected in the analysis of positive bar speeds alone. There were no significant differences in response speed to the negative bar.

SAL vs LSD.20

The two groups that were tested under the saline injection condition showed larger DRSs than the two groups tested under the 0.20mg/kg LSD condition ($F = 4.64$, $df = 1,16$, $p<0.05$). The analysis of the positive bar speeds themselves revealed the same findings. Analysis of the negative bar speeds separately revealed that groups tested under the saline condition responded faster than groups tested under the 0.20 mg/kg LSD condition ($F = 4.75$, $df = 1,16$, $p<0.05$).

LSD.05 vs LSD.20

There was a significant training effect ($F = 18.24$, $df = 1,16$, $p<0.01$) but no significant testing effect and no significant interaction. The LSD.05-LSD.05 and the LSD.05-LSD.20 groups were not significantly different from eachother but the LSD.05-LSD.05 group showed a larger DRS than the LSD.20-LSD.05 group. The LSD.20-LSD.20 group exhibited a smaller DRS than the LSD.05-LSD.05 and the LSD.05-LSD.20 groups ($F = 21.07$, $df = 1,16$, $p<0.01$) but this former group was not significantly different from the LSD.20-LSD.05 group. The analysis of the positive bar data alone revealed the same findings. There were no significant differences between the 4 groups in performance on the negative bar.

Differences in the overall weight of the subjects in the nine groups were tested for significance at the 0.05 level by applying the *t*-test. The groups did not show significant differences in weight relative to each other over the course of the experiment.

DISCUSSION

The results of the testing phase of the experiment suggest that high doses of LSD have an adverse effect on performance whereas low doses of LSD facilitate learning and performance. A facilitation of acquisition in an avoidance situation has been reported by Bignami [16]. The contention that high doses of LSD effect performance variables only is supported by the significant testing effect for the saline-high dosage analysis. Groups tested under high doses of LSD showed a significantly smaller DRS than groups tested under saline regardless of training phase injection condition. In addition, the SAL-LSD.20 group showed an immediate performance decrement after being switched to the high drug dosage. Learning effects are suggested primarily from the superior performance of the group maintained on the low dose contrasted with the saline group switched to the low dose. This latter group (SAL-LSD.05) however was not superior to the SAL-SAL control group in testing although it did improve its performance and finished the testing phase with higher DRS score than the SAL-SAL control. More training phase trials appear to be necessary to bring animals to asymptote in order to make the ensuing behavioral changes more readily detectable.

The data from the 3 unswitched groups of subjects indicate that LSD has biphasic effects on food maintained behavior with low doses facilitating discrimination performance and high doses impairing performance relative to placebo controls. In view of the previous literature these results could be interpreted as indicating that LSD in low doses, in addition to its effect on learning, produces an increased arousal or readiness to respond whereas high doses of LSD lead to a performance decrement because animals are more easily distracted by internal and external stimuli.

The analysis of the performance of the 3 unswitched groups in the testing phase also suggests that low and high doses of LSD produce their effects primarily through action on the positive stimulus. It is conceivable therefore that the drug changed the perceived value of the reward or that it attenuated the generalization of inhibition from the negative stimulus. However, it should be noted that the negative bar was withdrawn if a subject did not complete the FR 20 within 30 sec. It is possible that the use of a 30 sec limit on negative bar availability attenuated group differences on S− performance. Halasz and Marrazzi [11] have reported that low doses of LSD given to cats in a similar

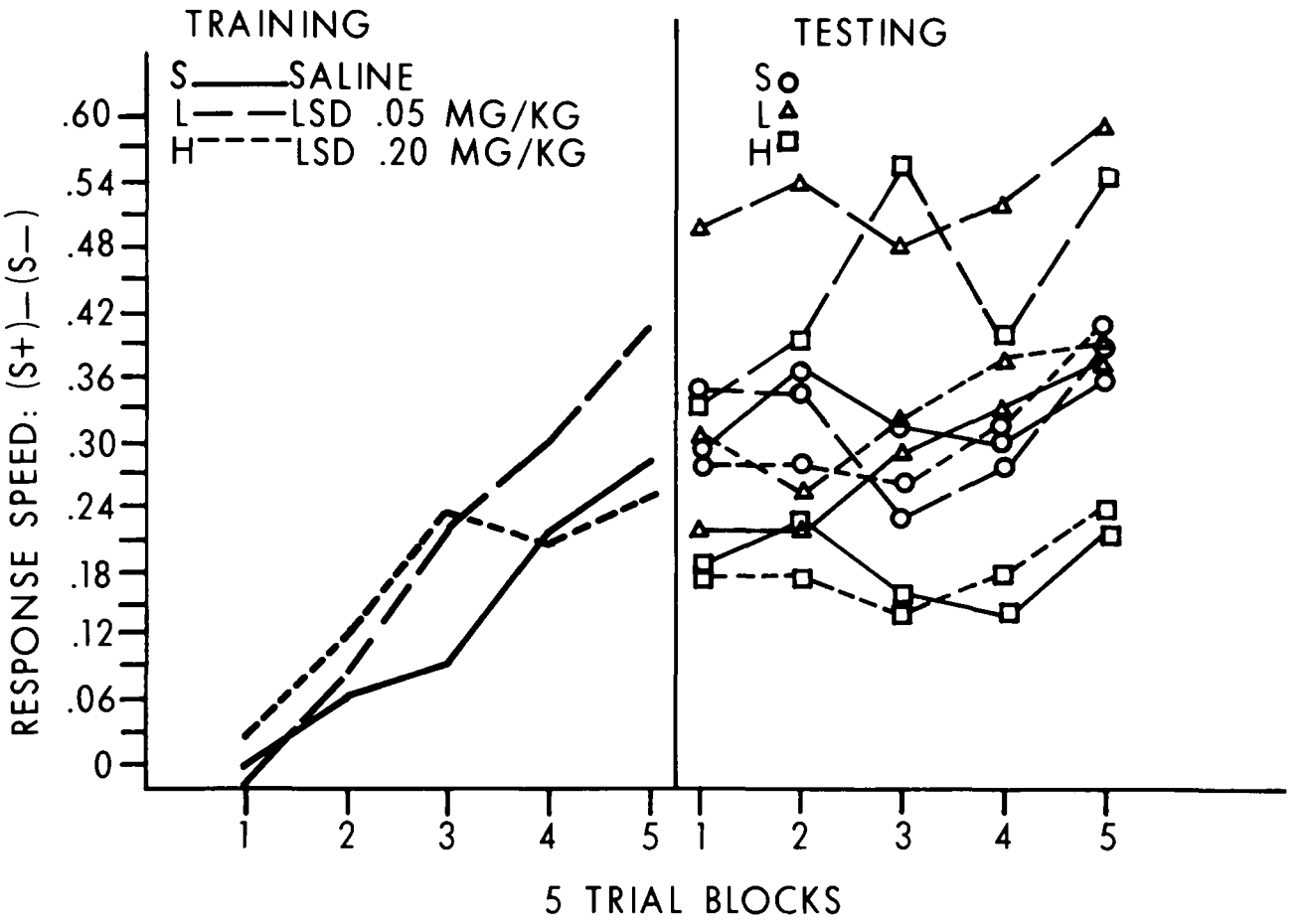

FIG. 1. Differential response speed (1/latency) to the first bar press for the three training groups (N = 15) and the nine testing groups (n = 5) as a function of 5 trial blocks. In testing, the symbols (○, △, □) refer to the test injection condition (Saline, Low or High dose) and the lines (——, - - -, - - - -) refer to the training injection condition (Saline, Low or High dose).

discrimination procedure increased responding to the negative stimulus.

A number of investigators, using similar LSD dosages, did not report behavioral facilitation [7,13] but the conflicting results may be due to the different behaviors that were studied. Animals in the present experiment were required to discriminate between a right and left lever whereas subjects in the above studies were reinforced for ratio or interval responding to a single stimulus. Jarrard [13], however, found that injections of 0.05 mg/kg LSD increased the number of responses emitted during a variable interval schedule of reinforcement and higher doses decreased operant responding. Behavioral facilitation with low doses of LSD in studies involving discrimination tasks has been reported by Blough [6] and Becker, Appel and Freedman [4] using pigeons, and by Meltzer [18] and Dykstra and Appel [9] using rats.

It is evident from Fig. 1 that all three groups learned the discrimination by the end of the training phase although, in the case of the low dose group, asymptotic performance had not yet been reached. These data are in accord with those reported by Dykstra and Appel [9] who found no alteration of stimulus control in a discrete trial auditory discrimination in rats using doses (0.04 and 0.16 mg/kg) comparable to those used in the present study.

Another interesting aspect of these data derives from the performance of the groups that were switched from one dose of LSD to another. The LSD.20-LSD.05 group did not show any facilitation in testing compared to the saline controls and the LSD.05-LSD.20 group did not show any response impairment. Thus high LSD doses given in training seem to prevent lower doses from exercising their positive effects although in this case it may simply be the effects of the training itself. More interesting is the fact that the debilitating effects of the high dosage were prevented by low dose training. The effect does not seem amenable to a simple training interpretation since SAL-LSD.20 animals showed immediate and prolonged response impairments. This quite clearly demonstrated the persistence of training variables into the testing phase.

EXPERIMENT 2

METHOD

Animals

Forty-five naive, male albino rats (Holtzman Co.,

Madison, Wisc.) approximately 90 days old and weighing between 325 and 375 g were used.

Apparatus

A wooden, straight alley, with interior dimensions of 73 in long x 4 1/2 in wide x 5 1/2 in high was used. The entire alley was painted flat black and was covered by Plexiglas hinged 3 1/2 in above the floor. Start and goal boxes were partitioned by means of two aluminum guillotine doors, one 12 in and the other 59 in from the beginning of the alley.

Start, run and goal times were measured by means of a microswitch coupled to the start gate and three photocell assemblies 5 in., 38 in. and 50 in. from that gate appropriately wired, through BRS solid state circuitry, to three Hunter Klockounters.

Procedure

Upon arrival animals were placed in individual cages and given ad lib food and water for 3 days. On Days 4 and 5 all animals were weighed, marked and randomly assigned to one of 3 groups of 15 each and placed on a 23 hr food deprivation schedule comparable to that of Experiment 1. The three injection conditions were: saline, 0.05 mg/kg LSD, and 0.20 mg/kg LSD. The LSD solutions were prepared from the tartrate salt (75.1% LSD by weight) in saline, so that the injection volume was 2 ml/kg, and all injections were IP. Solutions were kept frozen when not in use.

On Days 6–10 each animal was handled daily. On Days 11–15, the animals were given 5 direct placements into the goal box with five 0.045 g Noyes food pellets in a small coaster present on each placement. No injections were given during this pretraining phase. Training trials began on Day 16. Each weekday one of 5 squads was run for 15 trials. A squad consisted of three animals from each group. One week separated these experimental sessions for each squad. Over the course of 3 weeks all animals completed 45 training trials. On any given running day animals were injected 10 min prior to the first trial. Three animals were injected at one time and the completion of the 15 trials typically was accomplished within 45 min to one hour. The intertrial interval (ITI) during the day's trials was approximately 3–4 min.

A trial consisted of placing an animal in the start box and opening the door when the animal oriented toward it. As soon as the animal left the start box, the door was closed behind it. When the animal entered the goal area the goal box door was closed behind it to prevent retracing. Reinforcement on each trial always consisted of five 0.045 g Noyes food pellets. Animals were fed for one hour after completion of their day's trials. Those animals not run on any given day were also fed for 1 hr at the appropriate time in order that the deprivation schedule be maintained for all animals throughout the course of the experiment.

Following the 45 training trials, each group (N = 15) was divided randomly into 3 subgroups (n = 5) with 1/3 of the animals remaining in the same injection condition and the other 2/3 switched to either of the alternative injection conditions. Each daily squad now consisted of one animal from each of 9 groups determined by the factorial combination of 3 training injection conditions and three testing injection conditions: SAL-SAL; SAL-LSD.05; SAL-LSD.20; LSD.05-LSD.05; LSD.05-LSD.20; LSD.05-SAL; LSD.20-LSD.20; LSD.20-LSD.05; and LSD.20-SAL. Thirty additional trials were run (testing) at 15 per day, one day per week per squad, for two weeks. Magnitude of reward, deprivation level, daily ITI, and injection times were identical to those used in the training phase.

The testing phase was followed by a 15 trial, one week, extinction phase in which all animals were injected one more time under the testing injection condition (9 groups). An empty foodcup was present in the goal box during these trials. All other parameters were identical to the testing phase.

RESULTS

Start, run and goal speeds (1/latency) are presented in Figs. 2, 3 and 4 respectively. Separate analyses of variance were performed on each of these measures, and within each measure separate analyses were performed on each phase of the experiment. Since, in this experiment, each measure yielded different results, all three are presented. Injection conditions in training and testing were considered as between subjects sources of variance and days (5 trial blocks) was considered as the within subjects source or variance or repeated measure. Training and extinction data were analyzed for three groups whereas testing was analyzed for nine groups.

Start Speed

Training. All groups improved over days and LSD produced a dose related decrease in start speeds as is evident in Fig. 2. The analysis revealed significant effects for injection condition ($F = 6.86$, $df = 2,36$, $p<0.01$), trials ($F = 43.28$, $df = 8,288$, $p<0.01$) and their interaction ($F = 1.91$, $df = 16,288$, $p<0.05$). Subsequent analyses revealed that high dosage animals were inferior to both saline animals ($F = 10.69$, $df = 1,28$, $p<0.01$) and low dosage animals ($F = 6.73$, $df = 1,28$, $p<0.05$) whereas these latter two groups did not significantly differ from each other ($p>0.05$).

Testing. There were no significant effects of training variables in the testing phase. Group performance was determined primarily by testing injection condition and training phase asymptote. As in training, LSD produced dose related decreases in starting speed ($F = 19.74$, $df = 2,36$, $p<0.01$) and animals continued to improve over trials ($F = 25.58$, $df = 5,180$, $p<0.01$). Subsequent analyses revealed that groups receiving high dosage in the test phase were inferior to both saline ($F = 32.41$, $df = 1,28$, $p<0.01$) and low dosage ($F = 17.81$, $df = 1,28$, $p<0.01$) groups. Once again these latter two sets of groups (L and S) were not significantly different from each other ($p>0.05$).

Extinction. Figure 1 presents extinction data collapsed across training phase conditions since there were no training phase effects in either testing or extinction. It is clear from Fig. 1 that high dosage animals responded more slowly across extinction trials than did animals in the other conditions. However high dosage animals improved over the course of the extinction day whereas saline and low dosage animals showed marked performance declines with saline groups extinguishing somewhat more rapidly than low dosage groups.

Overall analysis of variance for the nine groups revealed a significant testing conditions effect ($F = 10.44$, $df = 2,36$, $p<0.01$), a significant trials effect ($F = 5.23$, $df = 2,72$, $p<0.01$) and a significant interaction of these two variables ($F = 5.27$, $df = 4,72$, $p<0.01$).

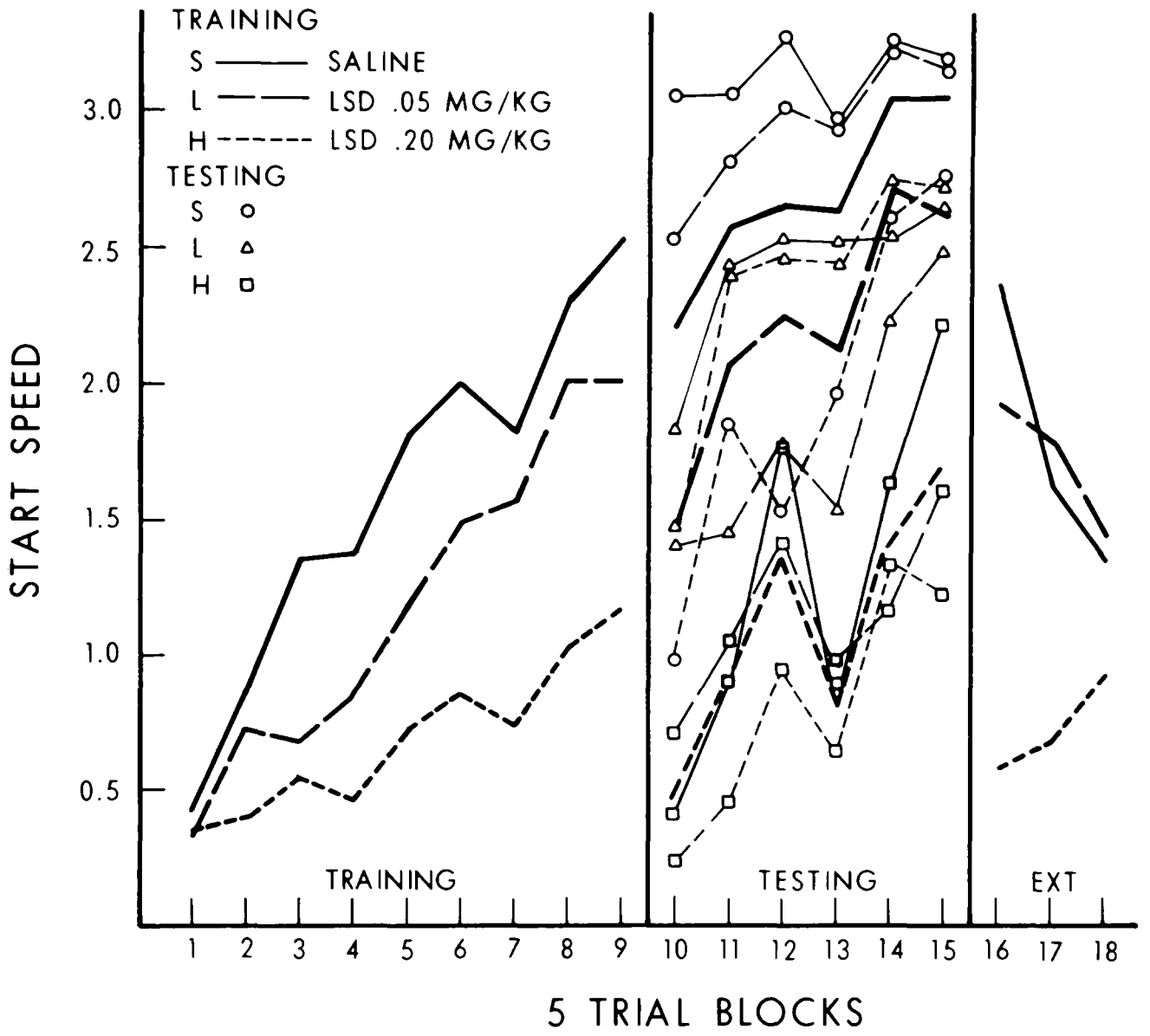

FIG. 2. Start speed (1/latency) as a function of 5 trial blocks for training, testing and extinction phases. The heavy lines represent all animals that received a particular injection (S, L or H) for that phase regardless of prior injection history.

Run Speed

Training. On this measure too all groups improved over trials and there was a dose related performance decrement. The differences were not, however, as large as those for start speed as is evident in Fig. 3. The analyses revealed overall effects of injection condition ($F = 3.73$, $df = 2,36$, $p<0.05$), trials ($F = 79.51$, $df = 8,288$, $p<0.01$), and their interaction ($F = 2.64$, $df = 16,288$, $p<0.01$). Subsequent analyses revealed that high dosage subjects differed from both saline ($F = 5.82$, $df = 1,28$, $p<0.05$) and low dosage ($F = 4.60$, $df = 1,28$, $p<0.01$) animals. In addition, a saline vs low dosage interaction ($F = 2.56$, $df = 8,224$, $p<0.05$) suggested that low dosage animals were responding significantly more slowly than saline animals over the last training day.

Testing. Once again training phase variables had little or no effect on test phase performance. Animals that received high doses in testing performed more poorly than low dose subjects which in turn were slower than saline animals. The overall analysis revealed effects of test injection conditions ($F = 19.05$, $df = 2,36$, $p<0.01$), and trials ($F = 32.24$, $df = 5,180$, $p<0.01$). There was in addition a significant triple interaction ($F = 2.03$, $df = 20,180$, $p<0.01$) between training conditions, testing conditions and trials. Subsequent analyses collapsed across training conditions revealed that high dosage animals performed more poorly than did low

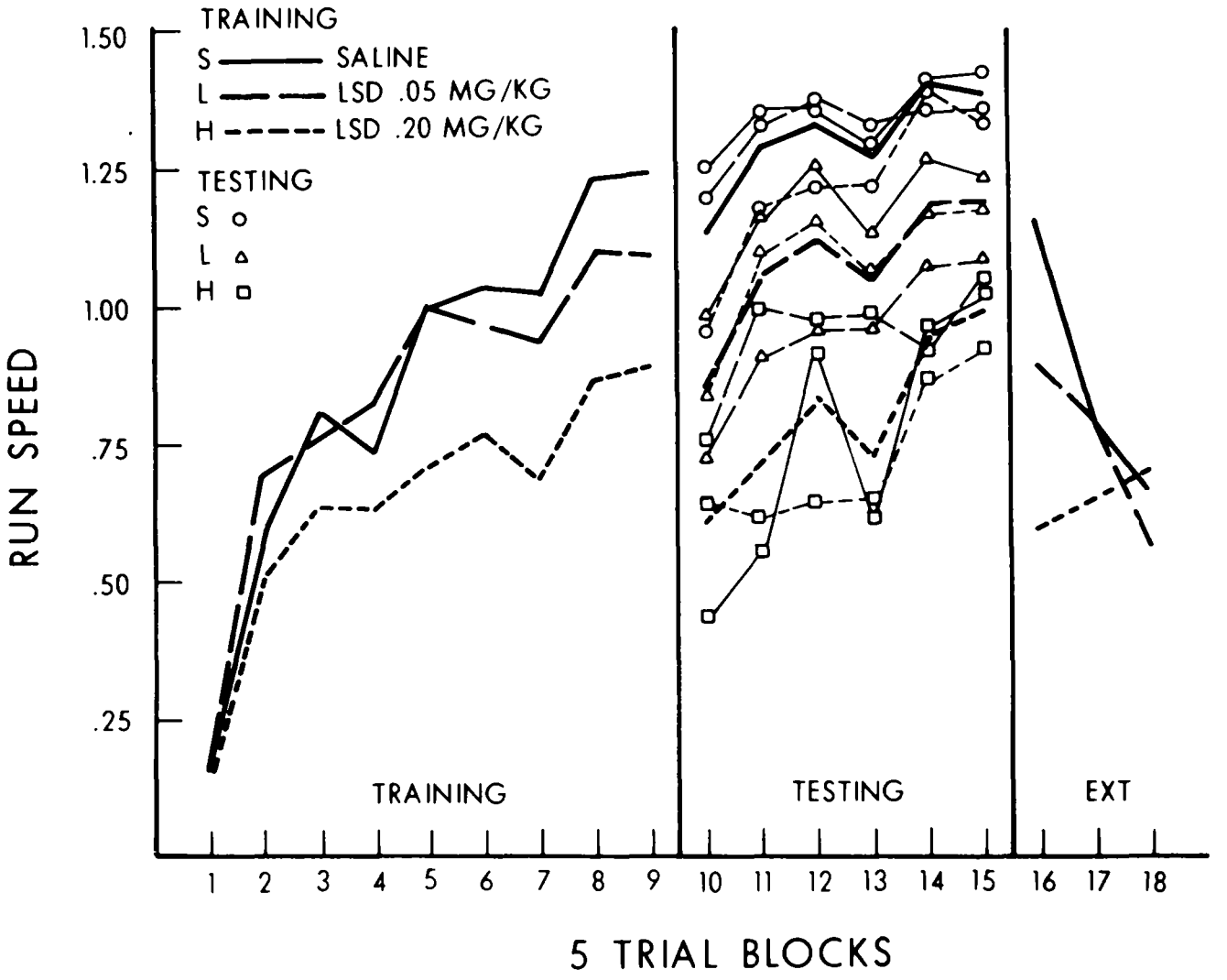

FIG. 3. Run speed (1/latency) as a function of 5 trial blocks for training, testing and extinction phases. The heavy lines represent all animals that received a particular injection (S, L or H) for that phase regardless of prior injection history.

dosage animals ($F = 9.02$, $df = 1,28$, $p<0.01$) and low dosage animals in turn performed more poorly than did saline animals ($F = 9.86$, $df = 1,28$, $p<0.01$).

Goal Speed

Training. All groups (Fig. 4) improved over trials ($F = 83.30$, $df = 8,288$, $p<0.01$) and, in marked contrast to the start and run speed data, there were no significant differences between the groups ($p>0.05$).

Testing. Groups given saline in testing generally performed somewhat better than groups given either low or high dosage although the differences between groups were much smaller than for start or run. There were significant effects of test injection conditions ($F = 3.27$, $df = 2,36$, $p<0.05$) and trials ($F = 15.99$, $df = 5,180$, $p<0.01$). In addition, there was a significant triple interaction of training x testing x trials ($F = 2.58$, $df = 20,180$, $p<0.01$).

Extinction. High dosage animals were clearly more resistant to extinction than either low dose or saline animals which did not differ from each other. The overall analyses revealed significant effects of extinction (i.e., testing) injection condition ($F = 10.41$, $df = 2,36$, $p<0.01$), trials ($F = 25.76$, $df = 2,72$, $p<0.01$), and their interaction ($F = 8.95$, $df = 4,72$, $p<0.01$). No other effects reached significance.

DISCUSSION

Unlike the previous study (Experiment 1), both low and high doses of LSD produced behavioral impairments to the extent that drugged animals ran more slowly than placebo animals in a dose-related fashion. These data on appetitive conditioning may be contrasted with the aversive situation in which faster running speeds to escape from shock have been reported with LSD [12]. There was no evidence of any biphasic effects.

The rather severe deterioration of start speeds compared to the moderate and minimal deteriorations in run and goal speeds respectively suggest an explanation in terms of stimulus generalization. At the outset it might be tempting

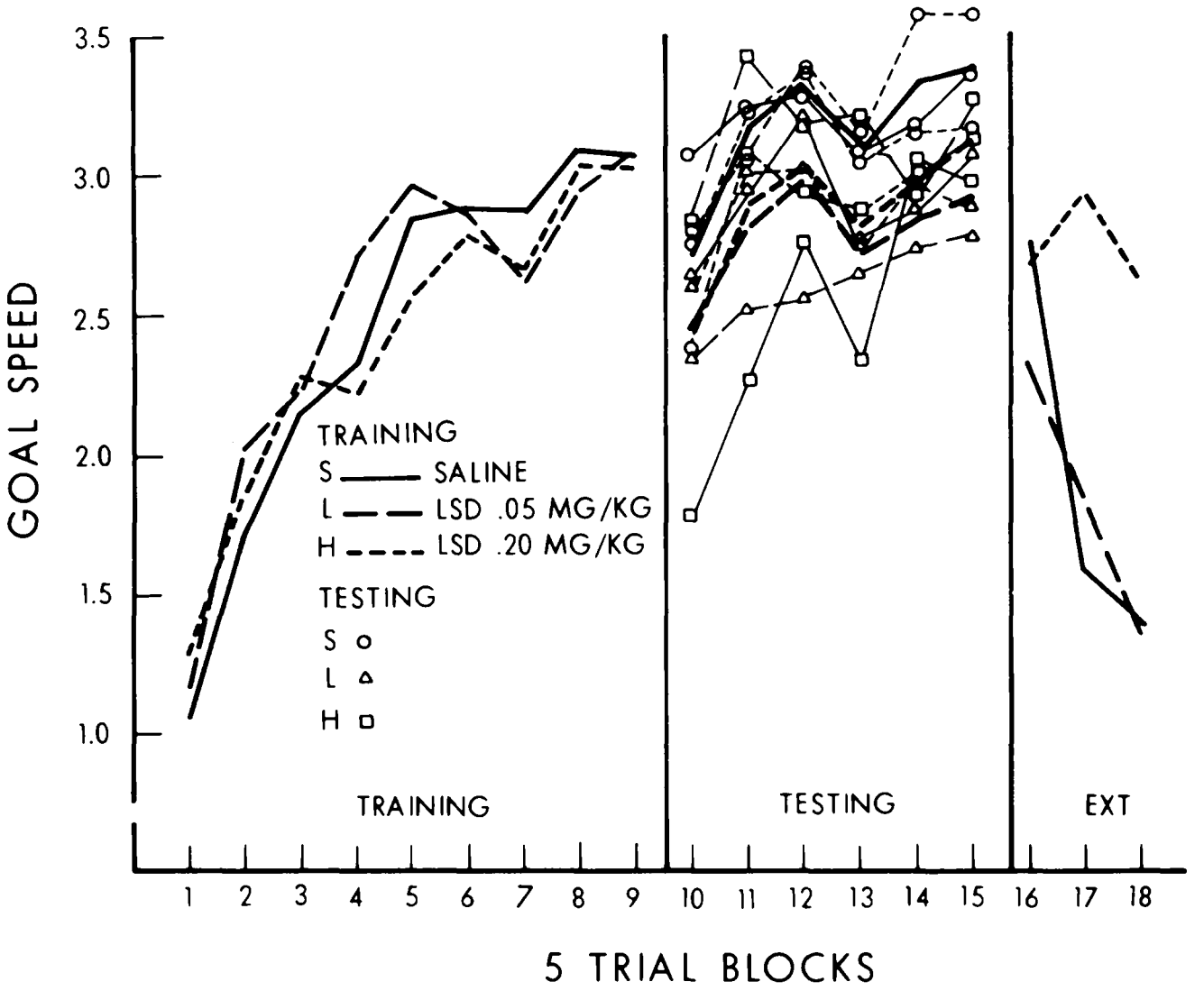

FIG. 4. Goal speed (1/latency) as a function of 5 trial blocks for training, testing and extinction phases. The heavy lines represent all animals that received a particular injection (S, L or H) for that phase regardless of prior injection history.

to explain the start speed effects simply in terms of drug-induced distraction or enhancement of competing behaviors elicited by the opening of the start door or an interference with the habituation process related to this repetitive stimulus. Key [15] has reported that LSD increased the reaction time of cats trained to avoid shock in the presence of a visual CS when distracting tones were presented but that LSD decreased reaction time in the absence of distracting stimuli. However, the fact that run speeds too were affected by the drug suggests that this explanation of the data is inappropriate. Indeed these effects argue against any explanation in terms of an impairment of general arousal or general peripheral changes and further suggest that the response impairment obtained in Experiment 1 with the high LSD dose was not simply a function of general toxicity. The enhancement of extinction performance also supports this notion. An alternative interpretation might focus on the differential effects of the drug as representing an impairment of stimulus generalization. Studies using auditory signals have failed to obtain changes in generalization slope with LSD [9], but there are reports of a change in visual stimulus generalization [1]. In Experiment 1 these effects on generalization may have been confounded by the use of both positive and negative stimuli and the mutual generalization of excitation and inhibition that they generate.

The present data may be directly contrasted with an identical study that used Cinanserin, a potent serotonin antagonist, rather than LSD [20]. In that experiment no differential effects on start, run and goal speeds were obtained with either of the doses used (12 and 36 mg/kg). LSD thus appears to be much more selective in its behavioral effects than Cinanserin and less open to the criticism of producing its effects through general toxicity. Whether or not these differences reflect differential interactions with a central tryptaminergic system is, of course, still open to question.

The increased resistance to extinction observed in the

present study conforms to earlier reports of response perseveration under LSD [7]. These data might also reflect decreased frustration or drive modulation [16] under the drug together with an attenuation of the capacity to relearn competing responses. It is unlikely, however, that the drug is simply interfering with the animal's ability to discriminate acquisition from extinction or presence vs absence of reinforcement since in Experiment 1 high dose animals were clearly capable of making such a discrimination.

With regard to the learning vs performance distinction, the major effects of the drug appear to be on performance, although the adjustment of the group that received high dose in training and saline in testing was relatively slow. The immediate deterioration of the saline-high group, however, argues for a strong performance effect of the drug. Once again these data may be contrasted with those previously reported for Cinanserin in which no learning effects of any kind were obtained.

GENERAL DISCUSSION

(1) A biphasic effect of LSD was observed in spatial discrimination learning but not in simple instrumental conditioning which suggests that task requirement are important determinants of LSD dose-response interactions.

(2) LSD increased resistance to extinction, an effect that is more aptly interpreted in terms of response perseveration than drive modulation or an attenuation of inhibition or frustration since no effect on the negative stimulus in discrimination learning was obtained.

(3) The differential effects of LSD on start, run and goal speeds in Experiment 2 suggest that some of the drug's performance effects may be related to stimulus generalization deficits.

(4) The slow response adjustments made by the group switched from high LSD dose to saline in Experiment 2 and the absence of rapid response improvements in the group switched from saline to low LSD dose in Experiment 1 suggest that the drug affected learning as well as performance.

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