Psychopharmacologia (Berl.) 34, 289–307 (1974)

Effects of LSD on Auditory Perception: A Signal Detection Analysis

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Received January 8, 1973; Final Version September 18, 1973

Abstract. The effects of LSD on perceptual behavior were analyzed with a signal detection procedure. This procedure is designed so that at least two of the parameters of a discrimination can be examined. The parameters examined were the physical properties of the stimuli being discriminated (e. g., sensory modality, discrimination difficulty) and the relative reinforcing properties of the environment (e. g., reinforcement probability). Two experiments were run. One experiment investigated the effect of LSD on the detection of tones of different frequencies, the other investigated LSD's effect on a temporal discrimination.

No dose or dosage regimen of LSD significantly altered the rat's ability to make the temporal or the frequency discrimination. LSD did, however, alter the rat's preference for responding on one of the two levers. The drug-induced alterations in lever preference were similar to the changes in lever preference which were produced by manipulating the reinforcement probabilities on the two levers. These changes were significant following doses of LSD greater than 0.04 mg/kg, and three doses of LSD given in a regimen designed to produce behavioral tolerance.

Key words: LSD — Discrimination — Temporal Discrimination — Signal Detection — Auditory Discrimination — Rats.

Introduction

While their very name suggests that hallucinogenic drugs, such as lysergic acid diethylamide (LSD), produce profound effects on perceptual experience and there are many reports that LSD alters perceptual behavior in both man (Hollister and Hartman, 1962) and lower animals (Appel, 1968), the nature of these effects is far from clear. Extensive investigations which have analyzed the effects of LSD on just one aspect of perception—that of the performance of well-established, sensory discriminations—have produced inconclusive results. For example, it has been reported that LSD may either increase (Becker, 1967; Blough, 1956, 1957a), decrease (Fuster, 1959; Key, 1961; Sharpe *et al.*, 1967; Siegel, 1969), or have no effect (Berryman, 1962) on the accuracy of

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relatively simple conditional discrimination problems such as matching to sample in animals.

There are several reasons for these and other conflicting results. First, different species, drug doses, and types of stimuli have been used in different experiments. Moreover, different stimulus dimensions (Blough, 1957b), response measures (Key, 1961), and levels of task difficulty (Polidora, 1963; Sharpe *et al.*, 1967; Uyeno, 1968) have also been found to influence drug effects. Available evidence also indicates that drugs affect perception in ways that depend on precisely *how* behavior is being controlled by a particular stimulus as well as by the physical characteristics of that stimulus (Dews, 1970; Terrace, 1963; Appel *et al.*, 1967; Appel, 1968; Key, 1961). That is, perceptual behavior, like any behavior, is controlled by parameters other than the physical characteristics of the stimuli being discriminated. One of those parameters is the consequences attached to the responses being made in a discrimination situation.

One way to study the effect of both the physical characteristics of the stimuli being discriminated and the consequences attached to making the discrimination is by adapting the methods of signal detection (Green and Swets, 1966) to the analysis of drug behavior interactions.

In this model any discrimination is said to involve both a problem of detecting a stimulus (sensitivity) and a problem of making a decision about how to respond to that stimulus (bias). This decision may vary according to factors that have nothing to do with the physical properties of the stimuli being discriminated—such as the consequences of the decision. Since a discrimination involves both sensitivity and bias factors, a drug can effect discriminatory behavoir in more than one way. For example, LSD may act as if it alters sensitivity (ability to detect a particular stimulus) or as if it alters bias (decision to respond in one way or another). In these experiments bias was manipulated by varying the reinforcement probability during discrimination performance, and sensitivity was manipulated by varying the difficulty of the discrimination.

Two experiments were run using a procedure in which two dimensions of auditory stimulation (frequency and duration) and three reinforcement probabilities (or different consequences) were studied. Both stimulus dimensions have been reported to be susceptible to modification by LSD (Hollister, 1968; Bradley and Elkes, 1959; Key, 1961; Altman and Appel, 1971; Appel, 1971). Behavior was measured over a large range of drug doses. In order to reduce the periods of no responding usually reported following intra-peritoneal (i. p.) administration of LSD, a procedure of drug administration which produces acute behavioral tolerance (Freedman *et al.*, 1964) also was used.

Methods

Subjects. The subjects were 12 male albino rats of Sprague-Dawley strain. At the beginning of each experiment they were approximately 120 days old and weighed 300 g. Their food intake was restricted to 10—12 g of Purina Laboratory Chow each day so that their weights remained at a relatively constant level. All animals were housed in a room kept on a 12-h, daynight cycle with constant temperature (78° F) and humidity (40—50%). Water was always available in individual home cages.

Apparatus. The apparatus consisted of Lehigh Valley chambers (Model 1316) and shells (LVE Model 1316C) equipped with two levers, located to the right and left of a liquid dipper which delivered 0.01 ml of sweetened milk. A dim overhead white house light, "white" noise and two green "feedback" lights directly above the levers were also provided. The box was modified in Experiment II to include a 6 inch chain which hung from the ceiling of the box and operated a microswitch.

Pharmacological Procedure. Lysergic acid diethylamide (LSD)[1] in a saline solution was administered intraperitoneally (i.p.) to each animal immediately before testing in doses of 0.04, 0.08, and 0.16 mg/kg, or according to a regimen of drug administration which was designed to produce acute tolerance. The order of drug injection was random. In the tolerance regimen, animals received three hourly does of 0.08 mg/kg of LSD, the third dose being given immediately before testing. A similar regimen of 3 doses of 0.13 mg/kg has been shown to produce tolerance to LSD-induced decreases in rate of responding, but not to other measures of drug effect (Freedman, *et al.*, 1964). Saline control injections of varying volume were given daily. Drug volumes varied from 0.12—0.50 cm^3.

Experiment I

Detection of Auditory Stimuli (Frequency Dimension)

Subject and Apparatus. Six rats were used. The tones used were between 2000 and 5000 Hz, the range in which the rat intensity threshold is relatively flat (Gourevitch and Hack, 1966). They were delivered through a 4″ Realistic speaker and two Hewlett-Packard Type 250 AB oscillators. The intensity of the various frequencies was measured inside the testing chamber with a H. H. Scott Type 450 Sound Level Meter and attempts were made to make the intensity level as equal as possible for each frequency (about 40 db re 0.002 dynes/cm were delivered by the oscillator and the Sound Lever Meter read between 70—80 db in the testing chamber).

Procedure. The rats were trained to respond differentially on a twolever auditory frequency discrimination task. Following an inter-trial interval during which barpressing on either of the two levers reset a timer which was set at 4 sec, one of the two stimuli was presented. The stimuli were tones of different frequencies. The tones remained on until the animal made one response on either lever. A response on the right lever in the presence of a "high" tone and a response on the left lever in the presence of a "low" tone were arbitrarily chosen as "correct" for three of the animals. For the other three, a left response was correct in the presence of a high tone and a right response in the presence of a low tone. The opposite responses were incorrect. Each incorrect response was followed by a 4-sec time-out, during which the box was dark. Correct responses were followed by the brief illumination

1 LSD was in the form of 0.1 mg/kg ampules manufactured by Sandoz Pharmaceuticals and obtained from the Center for the Study of Narcotic and Drug Abuse, National Institute of Mental Health.

Table 1. Testing conditions of Experiment 1

Discrimination	Reinforcement condition	Drug regimen (mg/kg LSD)
2000—5000	FR 10, 10	0.04, 0.08, 0.16, tolerance
	2, 10	0.04, 0.08, 0.16, tolerance
	10, 2	0.04, 0.08, 0.16, tolerance
3300—3800	FR 10, 10	0.04, 0.08, 0.16, tolerance
	2, 10	0.04, 0.08, 0.16, tolerance
	10, 2	0.04, 0.08, 0.16, tolerance
3000—4000	FR 10, 10	drug not given
	2, 10	drug not given
	10, 2	drug not given

of the lights above each lever (conditioned reinforcement). Milk reinforcement (accompanied by illumination of the lights above each lever) followed every tenth correct choice response, independently tabulated for each lever (FR 10, 10). After conditioned reinforcement, a new trial was initiated with the onset of the 4″ inter trial interval. The FR notation is used to designate the number of correct choice trials required for milk reinforcement. A noncorrection procedure was used. Whether the animal made a correct or incorrect response, the programmed series of high and low tones advanced to the next tone in the sequence. The sequence was random with each tone being presented approximately 50% of the time.

Three of the six animals were trained first on a 3300—3800 Hz discrimination, then on a 2000—5000 Hz discrimination and finally on a 3000—4000 Hz discrimination. This order was changed for the other three animals (1) 2000—5000, (2) 3000—4000, (3) 3300—3800 Hz. After stable base lines (criteria to be discussed below) were obtained for the FR 10, 10 schedule described above and drug was given, the reinforcement schedule was changed such that reinforcement occurred every tenth correct trial on one lever and every second correct trial on the other lever (FR 10, 2). Again, drug was given at this point. Later these values were reversed so that the FR 10 lever became the FR 2 lever and the FR 2 lever the FR 10 lever. A base line was obtained for each of these three reinforcement conditions at each of the three discriminations (2000—5000, 3300—3800, and 3000—4000 Hz) and drug was given under all conditions of the 2000—5000 discrimination and the 3300—3800 discrimination. No drug data was obtained for the 3000—4000 discrimination. 300 discrete trials were given each day and the number of correct and incorrect responses on each lever were recorded. Reaction times were also recorded. Table 1 summarizes the various testing conditions and drug regimens.

Experiment II

Detection of Auditory Stimuli (Temporal Dimension)

Subjects and Apparatus. Six rats were used. The apparatus has already been described (see General Methods, Experiment I).

Procedure. The rats were trained to emit a chain-pulling response which produced the temporal stimuli. They were then trained to respond differentially on a two-lever, temporal discrimination task in which the stimuli to be discriminated consisted of a 2.9 KHz tone with a duration of either 2.25 sec (long) or 1.25 sec

Table 2. Testing conditions for Experiment II

Discrimination	Reinforcement condition	Drug regimen (mg/kg LSD)
1.25/2.25-sec	FR 8, 8	0.04, 0.08, 0.16, tolerance
	FR 2, 8	0.04, 0.08, 0.16, tolerance
	FR 8, 2	0.04, 0.08, 0.16, tolerance

(short). The trial lasted until the animal made one response on either lever. For three of the animals a response on the right lever in the presence of the 2.25 sec tone and a response on the left lever in the presence of the 1.25 sec tone were correct. For the other three the opposite responses were correct. Incorrect responses were followed by a 4-sec time-out, during which the box was dark. Correct responses were followed by the brief illumination of the lights above each lever (conditioned reinforcement). Milk reinforcement (accompanied by illumination of the lights above each lever) followed every eighth correct choice response, independently tabulated for each lever (FR 8, 8). After conditioned reinforcement, a new trial was initiated with a chain-pulling response. The FR notation is used to designate the number of correct choice trials required for milk reinforcement. A noncorrection procedure was used. Whether the animal made a correct or incorrect response, the programmed series of long and short tones advanced to the next tone in the sequence. The sequence was random with each tone being presented approximately 50 % of the time.

After stable base lines were obtained, LSD was administered to each animal. The drug data were collected with the symmetrical reinforcement schedule (FR 8, 8). The schedule was then changed such that reinforcement occurred every eighth correct trial on one lever and every second correct trial on the other lever. Later, these values were reversed such that the lever with reinforcement every eighth trial became the lever with reinforcement every second trial and vice-versa. After base line data were obtained for each of these three sets of consequences (reinforcement frequencies), LSD was administered. Table 2 summarizes the various testing conditions.

Data Analysis

The results were examined in terms of receiver operator characteristic curves generated by the signal detection model (Green and Swets, 1966). An ROC curve is obtained in the following way: under a fixed stimulus condition, e. g., tones of 2000 and 5000 Hz, various sets of consequences, i. e., frequencies of reinforcement (e. g., FR 10, 2; FR 10, 10; FR 2, 10), are attached to the animals' responses. The probability of a left (or correct) response when one signal is present, p(Hit), and the probability of a left (or incorrect) response when the other signal is present, p(False Alarm), are determined for each of these sets of consequences. By sampling from a variety of testing conditions (i. e., reinforcement probabilities) and recording p(Hit) as a function of p(FA), a set of points emerges which when joined defines a response-conditional operating characteristic

(ROC) curve. Each point plotted represents the subject's performance in a given condition of the experiment, and each curve represents a different stimulus condition.

The ROC curve can then be used to obtain a measure of sensitivity and bias (lever preference). The area contained under a particular ROC curve is usually used in conventional signal detection analysis as a measure of sensitivity. For example, a curve in the upper left portion of the graph (Fig. 1) would contain an area close to 100% and is said to represent high sensitivity while the area contained under the major diagonal would be about 50%, representing chance level discrimination. It is also possible, however, to obtain an estimate of the area under a curve without making any assumptions about the shape of the theoretical curve. An index of sensitivity and bias can be determined for each individual point (or condition) according to a unit square analysis. This analysis has been used to measure both sensitivity (Pollack and Norman, 1964) and bias (Hodos, 1970) and formulas for determining these measures have been worked out (Grier, 1971). This type of analysis was used here so that measures of sensitivity and bias could be obtained for performance in each condition of the experiment without making any assumptions about the curve connecting these points.

In order to determine the sensitivity [called p(I)] at a given point, an estimate is made of the area contained under the possible curves that could pass through a given point. Points which have been generated under the same stimulus conditions should theoretically yield the same sensitivity value.

Bias is calculated in a similar manner. B'H, the bias measure, is an index of the distance along the ROC curve of a given data point from the negative diagonal (at which B'H = 0). A point far to the right of the curve would have a bias close to B'H = −1.00, and a point far to the left would measure a maximum bias of B'H = +1.00. When the reinforcement frequencies are symmetrical (FR 10, 10), the points obtained should be near the negative diagonal; with asymmetrical reinforcement conditions (FR 2, 10 and FR 10, 2), the points should approach the extremes of the curve.

Base lines for drug administration were based on stable values of both p(I) and B'H. Drug was not given unless p(I), the index of sensitivity, did not vary by more than 10% on the 3300—3800 discrimination of Experiment I [where p(I) measured about 0.65] and 5% on the 2000—5000 discrimination of Experiment I [where p(I) measured about 0.90] on three successive days. A 5-% variation was also used as the criterion for Experiment II. Variation in B'H, or bias, was allowed to reach as much as +0.20 from day to day (bias being measured in the range of −1.00 to +1.00) in both Experiments I and II.

The drug effect was measured by calculating changes in sensitivity, p(I), and bias, B'H. Since bias was allowed to vary more than sensitivity during control sessions, the following procedure was used to examine drug-induced changes in these measures. Data were obtained for each animal for three consecutive control days prior to each drug day. The difference in bias (B'H) and sensitivity [p(I)] between control day 1 and control day 2 (the measure of normal variability, called zero dose) was compared with the difference between control day 3 and drug day (the measure of drug induced variability). This method was used in order to determine whether the differences seen after drug administration were greater than changes which would be attributable to normal day to day variations.

Results

Experiment I

Fig. 1 shows three sets of ROC curves. Curves were obtained by plotting the probability of a left response (or correct response) when one tone was present [p(Hit)] and the probability of a left response (or incorrect response) when the other tone was present [p(False Alarm)]. These points were obtained at each of the three reinforcement conditions and for each discrimination. One curve was fitted (by inspection) to each set of three points obtained for each discrimination. It can be seen from this figure that the 2000—5000 discrimination produced a curve which runs close to the top coordinates of the graph—hit rate is high and false alarm low. As the tones were brought closer together, the curves approach the major diagonal where the hit and false alarm rates are equal. It can be seen here that different curves can be produced by altering the distance between the stimuli being discriminated. It can also be seen that the points obtained from each of the reinforcement conditions lie at similar positions along each curve. For the FR 10, 2 condition, the points lie along the far left side of the curve, with equal reinforcement probability (FR 10, 10), the points lie near the negative diagonal and with the FR 2, 10 condition, the points lie to the far right.

Tables 3 and 4 present the mean sensitivity and bias data obtained in Experiment I under control and drug conditions. Sensitivity, measured by p(I), was found to be a function of difficulty of discrimination. At the 2000—5000 Hz discrimination, the p(I) mean value was 0.88; at the 3000—4000 discrimination, it was 0.79 and at the 3300—3800 discrimination, it was 0.67. p(I) did not vary as the reinforcement probability was manipulated; bias, however, did reflect the probability of reinforcement. It also varied at the different discriminations. At the symmetrical reinforcement condition, bias was relatively close to zero; while at the assymmetrical conditions, animals were making more correct

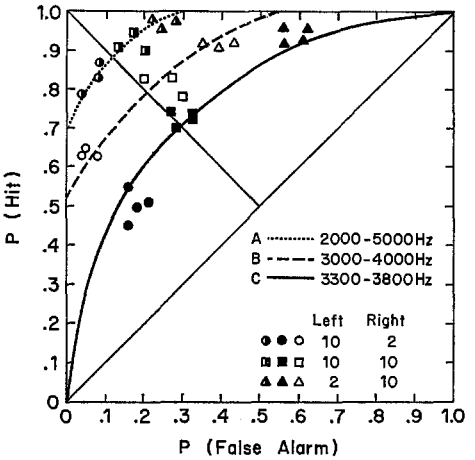

Fig. 1. Three receiver operator characteristic (ROC) curves for the performance of one rat on all three frequency discriminations of Experiment I. Points were obtained by plotting the probability of making a hit (i. e., responding on the left lever in the presence of a "high" tone) as a function of the probability of making a false alarm (i. e., responding on the left lever in the presence of a "low" tone). Points were obtained at each discrimination for three reinforcement conditions. In one reinforcement condition, every tenth correct response on the left lever and every second correct response on the right lever was reinforced with milk. In the second condition every tenth correct response on the left lever and every tenth correct response on the right lever was reinforced with milk. The third condition was the opposite of the first condition. Every second correct response on the left lever and every tenth correct response on the right lever was reinforced with milk. Conditioned reinforcement followed all correct response. The curves were fitted to these points by inspection

Table 3. Mean sensitivity [p(I)] values and standard deviations under drug and control conditions of Experiment I

Stimulus values	Drug dose (mg/kg LSD)	All reinforcement conditions	
		Mean p(I)	S. D.
3300—3800 Hz	0	0.67	0.05
	0.04	0.67	0.06
	0.08	0.66	0.05
	0.16	0.66	0.05
	0.08×3	0.67	0.07
3000—4000 Hz	0	0.79	0.04
		Drug not given	
2000—5000 Hz	0	0.88	0.03
	0.04	0.88	0.03
	0.08	0.85	0.07
	0.16	0.85	0.06
	0.08×3	0.86	0.05

Table 4. Mean bias (B′H) values and standard deviations under drug and control conditions of Experiment I

Stimulus values		Frequency of reinforcement					
	Drug dose (mg/kg LSD)	Left (10) Mean B′H	Right (2) S. D.	Left (10) Mean B′H	Right (10) S. D.	Left (2) Mean B′H	Right (10) S. D.
2000—5000 Hz	0	0.82	0.11	−0.05	0.12	−0.81	0.12
	0.04	0.84	0.08	−0.09	0.25	−0.72	0.10
	0.08	0.61	0.19	−0.12	0.18	−0.48	0.24
	0.16	0.51	0.32	−0.10	0.21	−0.61	0.11
	0.08×3	0.57	0.17	−0.12	0.45	−0.60	0.10
	0	0.73	0.09	−0.06	0.09	−0.66	0.11
		Drug not given					
3300—3800 Hz	0	0.45	0.11	−0.07	0.12	−0.59	0.18
	0.04	0.37	0.07	0.10	0.05	−0.51	0.20
	0.08	0.34	0.12	−0.11	0.17	−0.42	0.15
	0.16	0.18	0.22	−0.01	0.08	−0.40	0.18
	0.08×3	0.12	0.14	−0.03	0.14	−0.40	0.29

responses on the lever with the higher probability of reinforcement. When reinforcement probability was higher on the right lever, in the 2000 to 5000 Hz discrimination bias values were near +0.80; when left responses were reinforced with a higher probability, bias values shifted to −0.80. At the 3300—3800 Hz discrimination, the bias values shifted between +0.45 and −0.59 at the assymetical conditions.

Sensitivity [p(I)] and bias (B'H) were used to measure stability of discrimination behavior before drug administration. For the 3 days prior to drug administration, sensitivity [p(I)] was not allowed to vary more than 5% on the 2000—5000 discrimination and 10% on the 3300—3800 discrimination. Bias (B'H) was not allowed to exceed a change of +0.20. The drug effect was measured as a change in these measures. The difference between control day 1 and control day 2 was compared to the difference between control day 3 and the drug day for both the sensitivity and bias measures.

Four, two-way repeated measures analyses of variance were conducted—one analysis was done for each discrimination at which drug was given and for each measure (sensitivity and bias). The variables were reinforcement condition (FR 10, 10; FR 2, 10; FR 10, 2) and dose of LSD (0, 0.04, 0.08, 0.16 mg/kg and the tolerance regimen). The analysis showed no effect of differential reinforcement condition on either the sensitivity or the bias measure. There was, however, a significant effect of the dose of the drug on B'H on both discriminations [$F = 14.2$, $df = 4,89$, $P < 0.001$ (2000—5000); $F = 9.9$, $df = 4,89$, $P < 0.001$ (3300—3800)].

Fig. 2 shows the effect of three doses of LSD and the tolerance regimen on bias at the two discriminations at which drug was given (data being pooled from the three reinforcement conditions since analysis of variance showed no effect of reinforcement condition). At both discriminations, 0.08 and 0.16 mg/kg of LSD and the tolerance regimen produced significant changes in bias from zero dose. Analysis by *t*-tests was done to test for differences between zero dose and each of the four doses of LSD. Doses greater than 0.04 mg/kg of LSD and the tolerance procedure were significantly different from controls.

Since the main effect of a dose of LSD on sensitivity in the 2000 to 5000 discrimination suggested the possibility of a small effect, ($F = 1.3$, $df = 4,89$, $P < 0.2$) data from all the reinforcement conditions were pooled and *t*-tests were run between the zero dose (control) and each of the four doses of LSD. Only the differences obtained from 0.08 mg/kg of LSD and the tolerance regimen approached significance ($P < 0.10$). No dose or dosage regimen tested had this effect at the 3300—3800 discrimination.

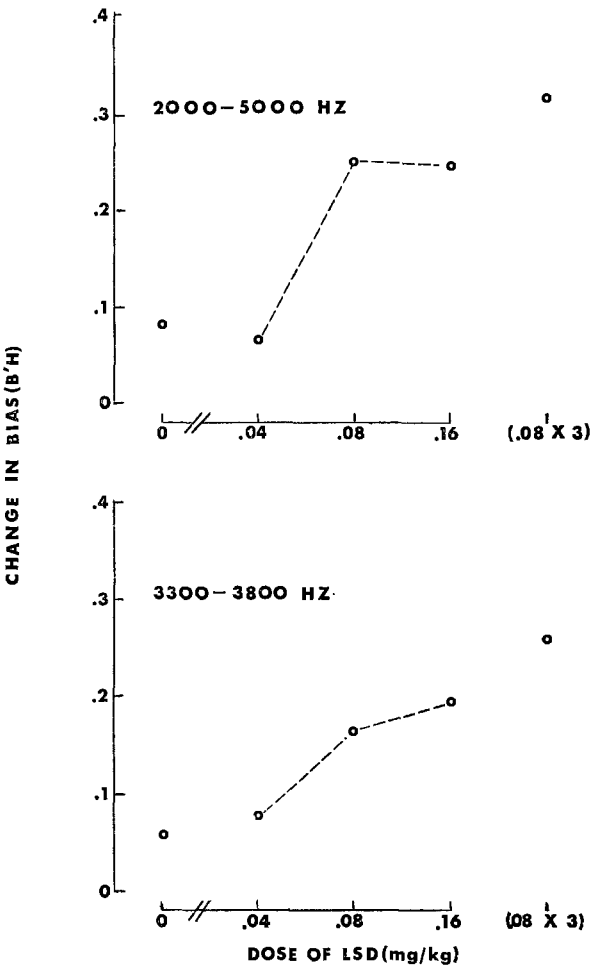

Fig. 2. Effect of three doses of LSD and a tolerance regimen on mean response bias from the six animals of Experiment I. Abscissa: dose. Ordinate: change in bias (B'H) between a control day and the following drug day. Zero dose represents the mean change in bias between two control days. Each point represents the mean of 3 observations in each of six rats

Fig. 3 shows the effect of 0.04, 0.08 and 0.16 mg/kg of LSD and the tolerance regimen on reaction time—i. e., the time from the onset of the tone until the animal responded. Sensitivity, p(I), did not vary as the reinforcement probability was manipulated, but bias, B'H, reflected the probability of reinforcement. This was true of all animals tested (not shown).

Tables 5 and 6 present the mean sensitivity and bias data in Experiment II under control and drug conditions. p(I) did not vary as the

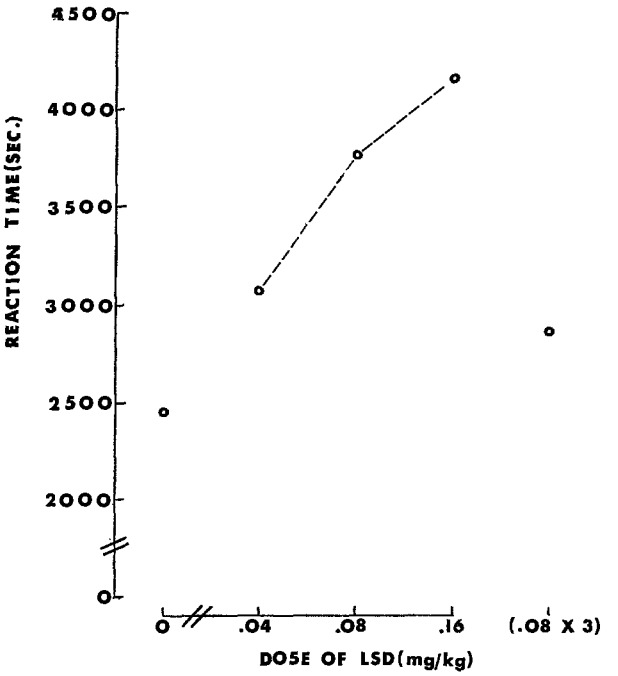

Fig. 3. Effect of three doses of LSD and a tolerance regimen on reaction time in the six animals of Experiment I. Abscissa: dose. Ordinate: reaction time from the tone onset until the animal responded on 1 of the 2 levers. Zero dose presents the mean reaction time for control days. Each point represents the mean of 6 observations in each of 6 rats

reinforcement probability was manipulated; bias, however, did reflect the probability of reinforcement. At the symmetrical condition, bias was relatively close to zero; while at the asymmetrical condition, it varied between $+0.70$ and -0.67.

As in Experiment I, p(I) and B'H were used to measure stability of discrimination behavior before drug administration. For the 3 days prior to drug administration, p(I) was not allowed to vary more than 5% and B'H was not allowed to exceed a change of ± 0.20. The drug effect was measured as a change in these measures. The difference between control day 1 and control day 2 was compared to the difference between control day 3 and the drug day for both the sensitivity and bias measures.

A two-way repeated measures analysis of variance was run on the sensitivity and bias data. The variables were reinforcement condition (FR 8, 8; FR 2, 8; FR 8, 2) and dose of LSD (0, 0.4, 0.08, 0.16 mg/kg and the tolerance regimen). As in Experiment I, the zero dose was

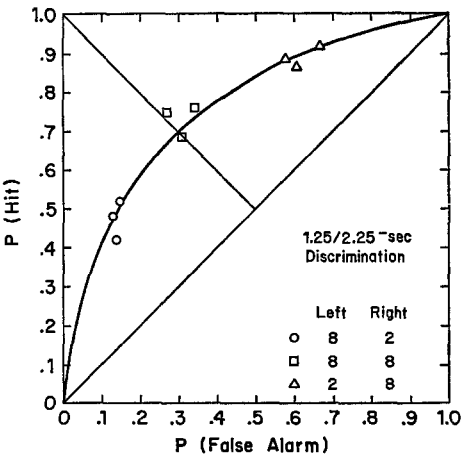

Fig. 4. One receiver operator characteristic (ROC) curve for the performance of one rat on the temporal discrimination of Experiment I. Points were obtained by plotting the probability of making a hit (i. e., responding on the left lever in the presence of a long tone) as a function of the probability of making a false alarm (i. e., responding on the left lever in the presence of a short tone). Points were obtained at each of the three reinforcement conditions. In one reinforcement condition every eighth correct response on the left lever and every second correct response on the right lever was reinforced with milk. In the second condition every eighth correct response on the left lever and every eighth correct response on the right lever was reinforced with milk. The third condition was the opposite of the first condition. Every second correct response on the left lever and every eighth correct response on the right lever was reinforced with milk. Conditioned reinforcement followed all correct responses. The curve was fitted to these points by inspection

Table 5. Mean sensitivity [p(I)] values and standard deviations under drug and control conditions of Experiment II

Stimulus values	Drug dose (mg/kg LSD)	All reinforcement conditions	
		Mean p(I)	S. D.
	0	0.77	0.09
	0.04	0.78	0.09
1.25 to	0.08	0.76	0.09
2.25 sec	0.16	0.73	0.10
	0.08×3	0.75	0.09

obtained by taking a mean of the four control-control differences obtained prior to each dose of the drug at each testing point. The analysis revealed no effect of reinforcement condition on the differences between control and drug variations for either sensitivity or bias. The drug had

Table 6. Mean Bias (B′H) values and standard deviations under drug and control conditions of Experiment II

Stimulus value	Drug dose (mg/kg LSD)	Left (8) Mean B′H	Right (2) S. D.	Left (8) Mean B′H	Right (8) S. D.	Left (2) Mean B′H	Right (8) S. D.
	0	0.70	0.14	0.11	0.15	— 0.67	0.20
	0.04	0.68	0.25	0.15	0.21	— 0.72	0.24
1.25—2.25 sec	0.08	0.65	0.11	0.18	0.08	— 0.42	0.23
	0.16	0.55	0.22	0.02	0.15	— 0.56	0.26
	0.08×3	0.52	0.23	0.05	0.21	— 0.58	0.25

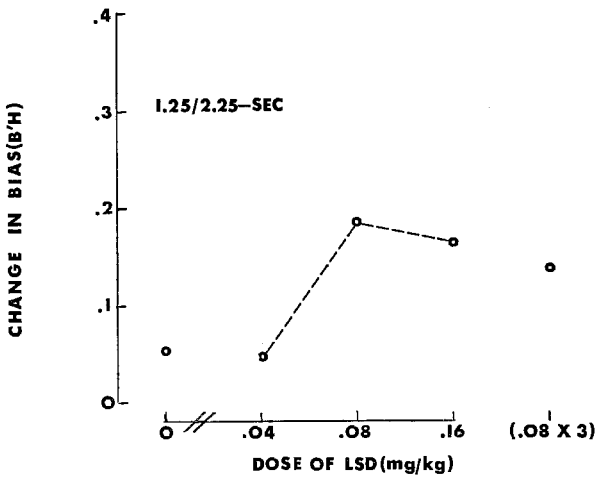

Fig. 5. Effect of three doses of LSD and a tolerance regimen on response bias in the six animals of Experiment II. Abscissa: dose. Ordinate: change in bias between a control day and the following drug day. Zero dose represents the mean change in bias between two control days. Each point represents the mean of three observations in each of 6 rats

significant effect on bias ($F = 14.1$, $df = 4,89$, $P < 0.001$) but not on sensitivity.

Since there was no main effect of reinforcement condition on bias, the data were pooled for all three reinforcement conditions, and t-tests were run to test for differences between zero dose (control) and each of the four doses of LSD. 0.04 mg/kg was not significantly different from zero dose, but 0.08 mg/kg, 0.16 mg/kg and the tolerance regimen all produced significant changes from control. Fig. 5 shows the effect of three doses of LSD and the tolerance regimen on bias.

The sensitivity scores were similarly pooled across reinforcement conditions and t-test were run to test differences between zero dose (control) and each of the four doses of LSD. Following 0.08 and 0.16 mg/kg of LSD changes approached but did not reach significance ($P < 0.10$).

Fig. 6 shows the effect of 0.04, 0.08, 0.16 mg/kg of LSD and the tolerance regimen on reaction time. Significant increases in reaction time following 0.08 and 0.16 mg/kg of LSD were revealed by t-tests. There were no consistent changes in premature responding.

Thus, as in Experiment I, significant changes in bias were seen under all testing conditions following all doses of LSD (0.08, 0.16 mg/kg and the tolerance regimen) except 0.04 mg/kg. Changes in sensitivity were not significant. Reaction time increased following the two larger doses of LSD (0.08 and 0.16 mg/kg), but not following the tolerance regimen.

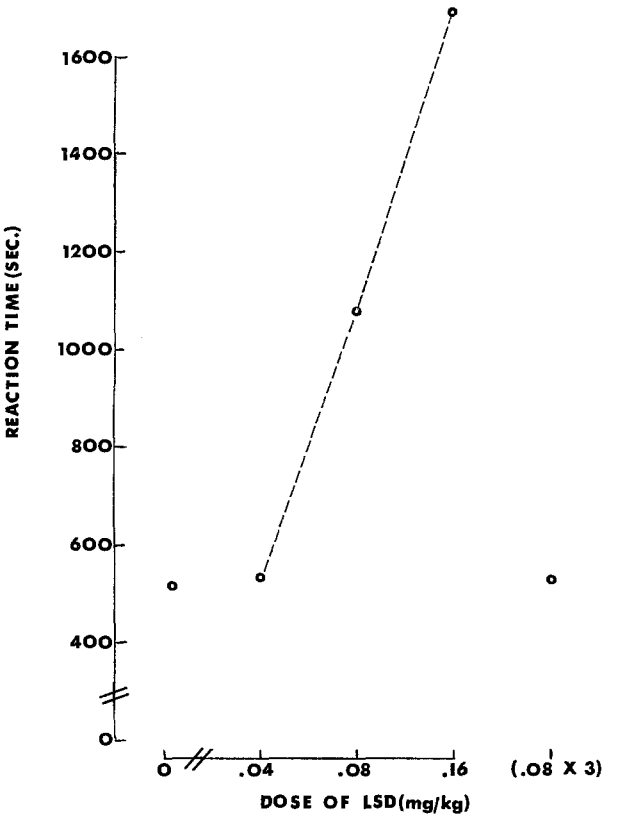

Fig. 6. Effect of three doses of LSD and a tolerance regimen on reaction time in the six animals of Experiment II. Abscissa: dose. Ordinate: reaction time from the beginning of each trial until 1. the animal pulled the chain to initiate the tone, 2. the tone remained on for its scheduled duration and 3. the animal responded on one of the two levers. Zero dose represents the mean reaction time for control days. Each point represents the mean of three observations in each of 6 rats

Discussion

In the experiments above, it was shown that LSD did not produce changes in sensitivity as measured by the rat's ability to make either a frequency or a temporal discrimination. Changes in sensitivity were obtained, however, by altering the distance between the stimuli presented for discrimination. Although no changes in sensitivity were seen following LSD administration, this is not to say that the rat may not be undergoing perceptual effects following LSD: Effects may be occuring to which these measures are not sensitive. Furthermore, the drug produces long periods of no responding—sometimes as long as 1 h. It is possible that drug

effects were occurring during these periods which were not being measured. It should be noted, however, that when a regimen of drug administration which produced tolerance to these periods of pausing or no responding was used, the results were identical to those obtained with a dose of LSD which produced pausing.

LSD did, however, produce consistent changes in bias under a variety of conditions of both Experiments. It was shown that a dose of 0.08, 0.16 and three doses of 0.08 mg/kg of LSD produced significant movement along the ROC curve generated by the signal detection model. Movement along the curve or change in bias was also found to occur when the reinforcement conditions were changed. Symmetrical conditions (equal reinforcement probability on both levers) produced bias close to zero, while the assymetrical conditions produced a preference for responding on the lever with the higher probability of reinforcement, which was reflected in high bias scores. Since the changes in bias produced by the drug were such that the animal exhibited less bias under drug than under control conditions, it might be said the drug acted as if it had altered the effect of reinforcement.

It is also important to note that B'H, when measured under control conditions, was much more variable than p(I), the measure of sensitivity. p(I) seldom varied by more than one or two percentage points; however, if B'H varied by as much as 0.20, the base line was still considered stable. Although there is no valid metric to express the strength of control, it might be said that bias was under less "control" than sensitivity. Therefore, it might be argued that the relative invariance of p(I) explains its resistance to drug-induced changes whereas B'H, because of its variability, was more easily affected by the drug. Although a significant trend was seen in the bias changes in that animals usually moved from a position of more to less bias under the drug, the drug also often produced large increases in the variability of the bias measure. This seems to indicate that LSD both attenuates the biasing effects of reinforcement as well as increasing the variability.

Finally, in each of the experiments above, consistent dose-dependent effects were found on the rate of responding following LSD. With a very low dose (0.04 mg/kg) decreases were seldom seen, but with both 0.08 and 0.16 mg/kg, LSD produced marked rate decreases. These rate decreases were usually seen as long periods (10—30 min) of pausing or no responding and are consistent with all reports that LSD in a comparable dose range produces decreases in response rate (Appel, 1968).

It should also be noted that while three doses of 0.08 mg/kg of LSD produced tolerance to drug-induced increases in reaction time, such as those seen following one dose of 0.08 or 0.16 mg/kg of LSD, no such tolerance occurred to the drug's effect on bias. Changes in bias following

the tolerance regimen of drug administration were similar to those changes seen following one large dose of LSD. Therefore, the occurrence of tolerance seems to depend on the particular measure being used to assess a drug's behavioral effect.

In conclusion, it was found that LSD did not significantly alter sensitivity in the rat as measured by a signal detection procedure. Bias was significantly different following LSD. Thus, LSD seems to alter the way in which environmental contingencies control perceptual behavior and has no effect on sensitivity at least in the situations described.

Acknowledgements. We wish to thank D. E. McMillan for comments on the manuscript. This research was supported by Research Grant MH 102-13-RD from the State of Illinois, Department of Mental Health, by Research Development Award USPHS 5 K2-MH-09355 (James B. Appel) and USPHS Pre-doctoral Research Fellowship 2-F01-48508 (Linda A. Dykstra) from the National Institute of Mental Health.

References

Altman, J. L., Appel, J. B.: The effects of LSD on fixed-interval responding in the rat. Paper presented at the meeting of the American Psychological Association, Washington, D. C., September 1971

Appel, J. B.: The Effects of "Psychotomimetic" drugs on animal behavior. In: Psychopharmacology: A review in progress. D. Efron, Ed., pp. 1211—1222. Washington, D. C.: U.S. Government Printing Office 1968.

Appel, J. B.: Effects of LSD on time-based schedules of reinforcement. Psychopharmacologia (Berl.) **21**, 174—186 (1971)

Appel, J. B.: Freedman, D. X., Filby, Y. M.: The effects of three psychoactive drugs on two varieties of escape behavior. Arch. int. Pharmacodyn. **167**, 179 to 193 (1967)

Appel, J. B., Whitehead, W. E., Freedman, D. X.: Motivation and the behavioral effects of LSD. Psychon. Sci. **12**, 305—306 (1968)

Becker, D. I., Appel, J. B., Freedman, D. X.: Some effects of LSD on visual discrimination in pigeons. Psychopharmacologia (Berl.) **11**, 354—364 (1967)

Berryman, R., Jarvik, M. E., Nevin, J. A.: Effects of pentobarbital, lysergic acid diethylamide and chlorpromazine on matching behavior in the pigeon. Psychopharmacologia (Berl.) **3**, 60—65 (1962)

Blough, D. S.: Some effects of drugs on visual discrimination in the pigeon. Ann. N. Y. Acad. Sci. **66**, 733—739 (1956)

Blough, D. S.: Effect of lysergic acid diethylamide on absolute visual threshold of the pigeon. Science **126**, 304—305 (1957a)

Blough, D. S.: Effects of drugs on visually controlled behavior in pigeons. In: Psychotropic drugs. S. Garattini and V. Getti, Eds., pp. 110—118. Amsterdam: Elsevier 1957b

Bradley, P. B., Elkes, J.: The effects of some drugs on the electrical activity of the brain. Brain **80**, 77—117 (1957)

Dews, P. B.: Studies on behavior: I. Differential sensitivity to pentobarbital of pecking performance in pigeons depending on schedules of reward. J. Pharmacol. exp. Ther. **113**, 393—401 (1955)

Freedman, D. X., Appel, J. B., Hartman, F. R., Molliver, M. E.: Tolerance to Behavioral effects of LSD-25 in rat. J. Pharmacol. exp. Ther. **143**, 309—313 (1964)

Fuster, J. M.: Lysergic acid and its effect on visual discrimination in monkeys. J. nerv. ment. Dis. **129**, 252–256 (1959)
Green, D. M., Swets, J. A.: Signal detection theory and psychophysics. New York: Wiley 1966
Gourevitch, G., Hack, M. H.: Audibility in the rat. J. comp. physiol. Psychol. **62**, 289–291 (1966)
Grier, J. B.: Nonparametric indexes for sensitivity and bias: Computing formulas. Psychol. Bull. **75**, 424–429 (1971)
Hodos, W.: Nonparametric index of response bias for use in detection and recognition experiments. Psychol. Bull. **74**, 351–354 (1970)
Hollister, L. E.: Human pharmacology of lysergic acid diethylamide. In: Psychopharmacology: A review in progress. D. Efron, Ed., pp. 1253–1261. Washingington, D. C.: U.S. Goverment Printing Office 1968.
Hollister, L. E., Hartman, A. M.: Mescaline, lysergic acid diethylamide and psilocybin: Comparison of clinical syndromes, effects on color perception and biochemical measures. Comprehens. Psychiat. **3**, 235–241 (1962)
Key, B. J.: The effect of drugs on discrimination and sensory generalization of auditory stimuli in cats. Psychopharmacologia (Berl.) **2**, 352–363 (1961)
Polidora, V. J.: A sequential response method of studying complex behavior in animals and its application to measurement of drug effects. J. exp. Anal. Behav. **6**, 271–277 (1963)
Pollack, I., Norman, D. A.: A non-parametric analysis of recognition experiments. Psychon. Sci. **1**, 125–126 (1964)
Sharpe, L. B., Otis, L. S., Schusterman, R. S.: Disruption of size discrimination in squirrel monkeys by LSD-25. Psychon. Sci. **7**, 103–104 (1967)
Siegel, R. K.: Effects of cannabis sativa and lysergic acid diethylamide on a visual discrimination task in pigeons. Psychopharmacologia (Berl.) **15**, 1–8 (1969)
Terrace, H. S.: Errorless discrimination learning in the pigeon: Effects of chlorpromazine and imipramine. Science **140**, 318–319 (1963)
Uyeno, E. T., Otis, L. S., Mitoma, C.: Behavioral evaluation of hallucinogenic trimethoxyamphetamines in squirrel monkeys (*Saimiri sciureus*). Communications in Behav. Biol. **1**, 83–90 (1968)

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