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LYSERGIC ACID DIETHYLAMIDE (LSD-25): I. PHYSIOLOGICAL AND PERCEPTUAL RESPONSES*

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A. INTRODUCTION

The purpose of this report is to present the variety and course of physiological and perceptual symptoms subjectively reported by "normal" human subjects reacting to various doses of lysergic acid diethylamide. The responses were elicited by means of a questionnaire containing 47 items. These items were compiled by going through the literature and listing the reported symptoms and signs, ostensibly due to LSD-25. The actual wording of the items in the questionnaire is listed in Table 2.

Early in our experiments it was discovered that certain subjects may give positive responses when only a placebo (tap water) was administered. In these subjects the scores on the questionnaire would make it appear that these subjects had actually been given LSD-25 instead of nothing at all. Indeed, the power of suggestion is so great that one of us (H.A.A.) has noted that an observer of the experiments reported more positive responses than the subject who had actually received LSD-25. To illustrate the nature of the responses under zero dosage of LSD-25, Table 1 summarizes five typical responses of subjects under our experimental conditions. Table 1A illustrates part of a questionnaire to aid the reader in understanding the way the items were scored. This was from Subject 12-64A (zero dosage). In the table, numbers 1-47 represent the questions of the questionnaire listed in Table 2. The response to the questionnaire as a function of time is shown for five separate subjects: 31-73B, 22-62C, 35-86B, 20-58B, and 12-64A. The experiments were performed as part of a group test. Note in the table that Subject 31-73B acted as an ideal subject. There were no positive responses to zero dosage during the entire experimental period of more than five hours. Subject 22-62C also shows only one positive response at one-half hour. In the case of Subject 35-86B the picture changes. There are now 12 different positive re-

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TABLE 1
POSITIVE RESPONSES TO QUESTIONNAIRE BY SELECTED SUBJECTS
UNDER ZERO DOSE OF LSD-25

(Five columns represent five separate subjects. Time, in hours after placebo, is indicated by numbers $\frac{1}{2}$ - $3\frac{1}{2}$.)

Question number	31-73B	22-62C	35-86B	20-58B	12-64A
	$\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ + $\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ + $\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ +	$\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ + $\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ + $\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ +	$\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ + $\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ + $\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ +	$\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ + $\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ + $\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ +	$\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ + $\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ + $\frac{1}{2}$ $1\frac{1}{2}$ $2\frac{1}{2}$ $3\frac{1}{2}$ $3\frac{1}{2}$ +
1					x
2					x
3			x		
4					x
5					x
6				x	x
7				x	x
8					
9				x	x
10					x
11					
12					
13					
14					
15			x		x
16			x		
17				x	
18					
19					
20					
21					
22					

TABLE 1a

TYPICAL RESPONSE TO QUESTIONNAIRE: BLANK SPACES INDICATE NEGATIVE RESPONSES (Half an hour after administration and at hourly intervals thereafter, the following direct questions are put to the subject. His rating is accepted, if possible on a + to +++++ basis)

Question	Up to ½ Hr.	Up to 1½ Hrs.	Up to 2½ Hrs.	Up to 3½ Hrs.
1. Do you feel ill in any way?	.	.	.	+
2. Are you nauseated?	.	.	.	+
3. Have you a feeling of choking?	+	.	.	.
4. Is salivation increased?	++	++	+	++
5. Or decreased?	+	+	.	.
6. Is your appetite increased?	+	++	+	.
7. Or decreased?	.	++	.	.
8. Do you have a "dry" taste in your mouth?	.	.	.	.
9. Do you have a funny taste in your mouth?	+	.	.	++
10. Is it a bitter taste?	.	.	.	++
11. Are your lips numb?	.	.	.	.
12. Or drawn back as if you were smiling?	.	.	.	.
13. Does your head ache?	+	+	+	++++
14. Are things moving around you?	.	.	.	.
15. Do you feel dizzy?	.	.	.	.
16. Or unsteady?	.	.	.	.
17. Is there difficulty in breathing?	.	.	.	.
18. Do you pass more urine than usual?	.	.	.	.
19. Are you aware of your heart beat?	.	.	.	.
20. Is it faster than usual?	.	.	.	.
21. Are you sweating?	.	.	.	.
22. Are you hot?	.	.	.	.
23. Or cold?	.	.	.	.
24. Are your palms moist?	++	.	.	.
25. Or dry?	.	.	.	.
26. Or cold?	.	.	.	.
27. Is your skin sensitive?	+	.	+	+
28. Do you have funny feelings on your skin?	++	.	.	+
29. Do your hands and feet feel peculiar?	++	+	.	++
30. Do they feel heavy?	++	++	.	.
31. Or light?	+	++	.	+++
32. Is there pressure in your ears?	+	+	.	++
33. Is your hearing abnormal?	++	+	.	++
34. Is it more acute than usual?	++	+	.	.
35. Is your eyesight blurred?	.	.	.	.
36. Do you have difficulty in focusing your vision?	.	.	.	.
37. Do you see double?	.	.	.	.
38. Are shapes and colors altered in any way?	.	++	.	+
39. Does light bother you?	.	.	.	.
40. Do things seem too close?	.	.	.	.
41. Or too far away?	.	.	.	+++
42. Do you tremble inside?	++	+	.	.
43. Do you feel weak?	.	.	.	.
44. Or fatigued?	.	.	.	.
45. Do you feel drowsy?	.	.	.	.
46. Do you feel as if in a dream?	.	.	.	++
47. Are you anxious?	+	+	+	++
	15	12	5	15

TABLE 2
AVERAGE PERCENTS OF SUBJECTS IN THREE LSD-25 DOSAGE GROUPS RESPONDING
POSITIVELY TO EACH QUESTION

Question Number	Question	Percent of subjects		
		N = 13 0 Gamma	N = 21 25-75 Gamma	N = 14 100-225 Gamma
1	Do you feel ill in any way?	8	11	24
2	Are you nauseated?	3	15	26
3	Have you a feeling of choking?	1	11	12
4	Is salivation increased?	9	15	6
5	Or decreased?	6	12	22
6	Is your appetite increased?	5	11	17
7	Or decreased?	11	14	19
8	Do you have a "dry" taste in your mouth?	5	17	16
9	Do you have a funny taste in your mouth?	8	19	19
10	Is it a bitter taste?	4	7	9
11	Are your lips numb?	1	16	21
12	Or drawn back as if you were smiling?	0	19	14
13	Does your head ache?	20	27	20
14	Are things moving around you?	0	9	17
15	Do you feel dizzy?	7	29	40
16	Or unsteady?	3	43	48
17	Is there difficulty in breathing?	3	9	7
18	Do you pass more urine than usual?	5	7	6
19	Are you aware of your heart beat?	2	17	7
20	Is it faster than usual?	5	10	8
21	Are you sweating?	1	17	18
22	Are you hot?	7	26	21
23	Or cold?	0	9	8
24	Are your palms moist?	35	45	41
25	Are your palms dry?	0	3	7
26	Or cold?	9	7	7
27	Is your skin sensitive?	4	11	18
28	Do you have funny feelings on your skin?	2	31	38
29	Do your hands and feet feel peculiar?	9	41	40
30	Do they feel heavy?	7	25	30
31	Or light?	2	23	24
32	Is there pressure in your ears?	4	20	24
33	Is your hearing abnormal?	4	12	3
34	Is it more acute than usual?	4	7	15
35	Is your eyesight blurred?	2	22	24
36	Do you have difficulty in focusing your vision?	0	14	27
37	Do you see double?	0	0	2
38	Are shapes and colors altered in any way?	1	11	14

TABLE 2 (*continued*)

Question Number	Question	Percent of subjects		
		N = 13 0 Gamma	N = 21 25-75 Gamma	N = 14 100-225 Gamma
39	Does light bother you?	2	8	6
40	Do things seem too close?	0	7	7
41	Or too far away?	0	8	13
42	Do you tremble inside?	6	40	47
43	Do you feel weak?	2	39	41
44	Or fatigued?	11	39	23
45	Do you feel drowsy?	24	34	28
46	Do you feel as if in a dream?	6	37	33
47	Are you anxious?	13	22	27

sponses, some of which were maintained during the entire period of the experiment even though no medication at all had been administered. Note especially that Subject 35-86B had responses especially characteristic of LSD-25 itself, e.g., eyesight blurring, seeing double, and visual distortions. The pattern becomes even more marked with Subject 20-58B, who throughout the experiment felt as if he were in a dream and had peculiar sensations in his hands and feet. Perhaps most striking of all of the group presented here is Subject 12-64A who responded positively to almost half of the items and whose symptoms persisted for approximately 10 hours. Indeed, Subject 12-64A had such a severe response to the placebo that considerable care was required to maintain an experimental situation that was not traumatic.

In view of the data presented in Table 1 it appears evident that previous studies reporting the effects of LSD-25 upon "normal" subjects need re-evaluation in terms of placebo (zero) dosage. Reference may be made to Rinkel, DeShon, and Solomon's (9) work, the investigations of Stoll (12), those of Savage (11), as well as others (1, 2, 3, 4, 5, 6, 7, 8, and 10), in which the use of controls given zero dosage was not perhaps as adequate as desirable. Indeed, it was found by us that for a given group of individuals suitable evaluation of responses to LSD-25 could not be made without the use of a zero dose control group. Further, at the time that this report was compiled there were no investigations in the literature which justify the conclusion that the symptoms reported, especially at low dosage, are significantly related to LSD-25 intoxication.

B. METHOD

1. General

The questionnaire, as mentioned in the Introduction, was constructed on the basis of the physiological and perceptual symptoms reported in the litera-

ture. After several revisions, the final form consisted of 47 questions so designed that a positive response indicated the presence of a given symptom (Table 2). The questions were asked by the observer one-half hour after the administration of the drug and usually at five hourly intervals thereafter.

While suggestibility could not be prevented under our conditions, it was partially controlled by having the same questions asked of each individual at each interval. Periodic questioning also enabled the evaluation of drug effects as related to time. Onset, peak, and decline of symptoms could also be fairly well determined.

Only positive and negative responses were analyzed, although graded responses were obtained.

The form of the questionnaire is illustrated in Table 1a.

2. *Sample*

The sample consisted of a group of 26 paid, adult volunteers. On the basis of the Rorschach, Wechsler-Bellevue Intelligence Scale, Bender Gestalt, House-Tree-Person, and Thematic Apperception tests, subjects were classified as non-psychotic or psychotic. Only those falling within the non-psychotic range were accepted as subjects. Fifteen males and 11 females were used. Ages ranged from 24 to 41 years and *IQ*'s from 100 to 137. Weights ranged from 103 to 203 pounds and height from 5 feet to 6 feet, 2 inches.

3. *Dose and Test Conditions*

Doses ranged from zero, in which subjects received only water, to 225 micrograms of lysergic acid diethylamide. At no time did the subjects know their dosage. Doses were divided into three categories: zero, low (25-75 micrograms LSD-25), and high (100-225 micrograms LSD-25). Thirteen subjects were tested at zero, 21 at the 25-75 microgram level, and 14 at the 100-225 microgram level. Six of the subjects received the drug at all three levels; five were tested at both the zero and 25-75 microgram level, but not at the 100-225 microgram level. Six subjects were tested at the 25-75 and 100-225 microgram levels but not at the zero level. Eight subjects were tested at only one level.

Subjects received the drug at about 10:30 or 11:00 A.M., several hours after breakfast. They were usually observed in groups of two, three, or four with the doses usually different amongst the subjects. Most of the time was spent in the experimental room where psychological and psychophysical tests were administered. Group discussions were conducted when the questionnaire was not being used.

4. *Analysis*

Responses to the questionnaire were analyzed in terms of responses to each of the 47 items, and the number of items to which positive responses were given. Within these two categories a number of analyses were made:

a. Item analysis.

(1). The percentage of subjects in each of the three dose groups responding positively to each question at each of the six hourly intervals was determined.

(2). The average percentage of subjects in each of the three dose groups responding positively per hour, over the five-hour period, was determined.

(3). Questions were ranked within each dosage group according to average hourly percentage response. A comparison of the three rank positions of questions was made.

(4). The questions which significantly discriminate between any two of the three dose levels were determined.

b. Number analysis.

(1). The average number of positive responses given during the experimental period to the 47 questions was determined for each of three dose groups. This was done for each of six hourly intervals, separately, as well as for the total five-hour period.

(2). The differences between dosage groups in number of responses made were analyzed to determine their statistical significance.

(3). Rank positions of subjects, according to average number of positive responses made per hour at each dose level, were compared as a means of evaluating the significance of the individual subject's rank.

(4). The number of responses made by subjects tested twice at the same dose level was compared to determine the consistency of response.

(5). The subject's body weight was correlated with the number of positive responses made at a given dosage.

C. STATISTICAL PROCEDURE, RESULTS, AND DISCUSSION

1. *Item Analysis*

a. Hourly response to each question.

(1). *Statistical procedure.* The 47 items on the questionnaire were subjected to analysis first by transferring the data from the questionnaire cards to IBM cards. The data were divided into three dosage groups: (a) zero micrograms LSD-25 in which there were 13 subjects who received only

water; (b) 25-75 micrograms LSD-25 in which there were 21 subjects, most of whom received 50 micrograms; and (c) 100-225 micrograms LSD-25, consisting of 14 subjects, most of whom received 100 micrograms. No subject appeared twice within any one of the three groups, although a number of the subjects appeared in two or three of the groups. In cases where a subject was tested at more than one dose within a dose group, data from the highest dose were always used. Where subjects were tested more than once at a given dose, data from the first test were used. In this way "weighting" of results was avoided.

The total number of positive responses made to each question by the subjects in each group at six hourly intervals was tabulated by means of the IBM 101 Electronic Statistical Machine. Although positive responses were originally made on a plus one to a plus five basis, it was felt that the evaluation was too subjective and the number of subjects too small to warrant separate analysis of each degree of plus response. Consequently, all plus responses were considered as positive responses and treated as equal.

The percentage responding positively each hour was then calculated by means of the following formula:

$$P = \frac{\sum_{i=1}^N X}{N} \times 100 \quad (1)$$

where P equals the percentage, $\sum_{i=1}^N X$ equals the sum of plus responses, and N equals the number of subjects in the groups

(2). *Results.* Figure 1, containing Items 1-47, and our discussion of items 1-47, indicates the percentage of subjects in the three dose groups giving positive responses to the items at each of the hourly intervals. The percentage of subjects responding positively to each question is placed on the ordinate of a co-ordinate system, and the time of response is placed on the abscissa. Each point represents the percentage response at a given time. The time curve of each question is shown on a separate graph.

In the following paragraphs the results shown in Figure 1 are briefly discussed.

Item 1: "Do you feel ill in any way?" For zero dosage, out of 13 subjects only 8 per cent responded positively in each interval, except for the fourth interval where two responded positively. In terms of percentages, the peak occurred at 3½ hours for zero dosage with 15 per cent responding posi-

tively. For a dosage of 25-75 micrograms the peak occurred at $2\frac{1}{2}$ hours with 19 per cent responding positively. For the dosages of 100-225 micrograms, when the peak occurred approximately $1\frac{1}{2}$ hours after the drug, 43 per cent responded positively. Thus, there was both a more rapid and marked effect from the highest dose of LSD-25, where almost half of the people reported feeling ill in the second hour. It is interesting to see that for this high dose the percentage of people feeling ill declined very rapidly after $1\frac{1}{2}$ hours.

Item 2: "Are you nauseated?" No one with zero dosage reported nausea

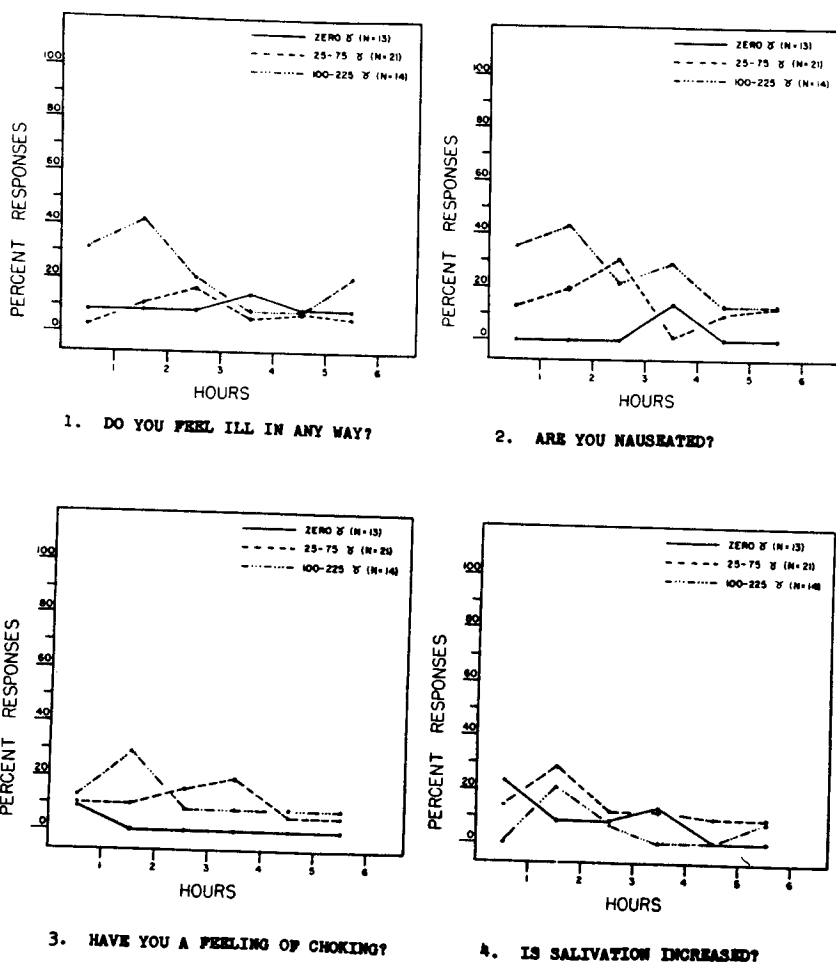
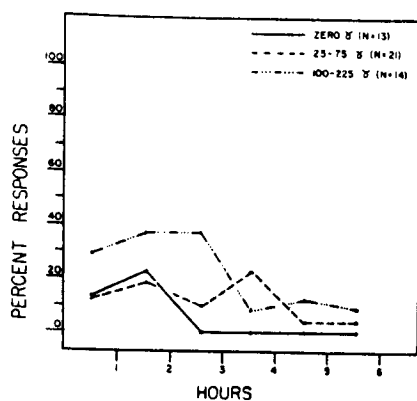


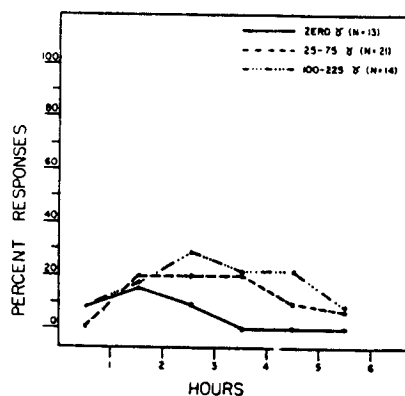
FIGURE 1
HOURLY RESPONSE TO EACH OF 47 QUESTIONS

until 3½ hours after the placebo, when 15 per cent reported this symptom. For the low dosage level, 25-75 micrograms, the peak number of responses occurred at 2½ hours when 29 per cent of the subjects reported feeling nauseated. Forty-three per cent of the subjects receiving 100-225 micrograms of the drug, reported feeling nauseated 1½ hours later.

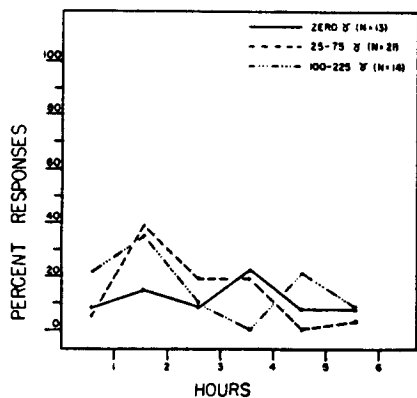
Item 3: "Have you a feeling of choking?" There was only one positive response (or 8 per cent) for the first interval for those receiving no LSD-25. Those receiving the low dosage gave the maximum number of responses after 3½ hours when 19 per cent of the subjects gave positive responses. For



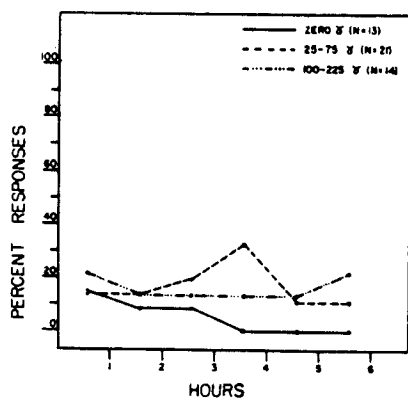
5. IS SALIVATION DECREASED?



6. IS YOUR APPETITE INCREASED?



7. IS YOUR APPETITE DECREASED?



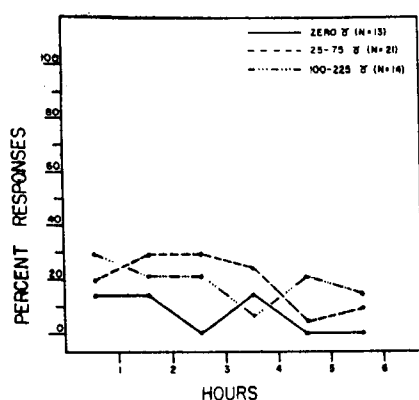
8. DO YOU HAVE A "DRY" TASTE IN YOUR MOUTH?

FIGURE 1 (continued)

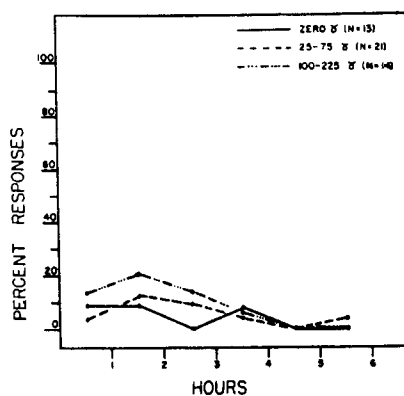
the high dosage the peak was again reached in the second interval ($1\frac{1}{2}$ hours) and the percentage giving positive responses was 29. The high dosage of LSD-25 again showed greater and more rapid positive response.

Item 4: "Is salivation increased?" Among those receiving no LSD-25, 23 per cent reported that their salivation was increased $\frac{1}{2}$ hour after the placebo. About 29 per cent of the subjects receiving the low dosage reported that their salivation was increased in the second interval. This was also the peak hour for the 100-225 microgram group, when about 21 per cent reported that their salivation was increased.

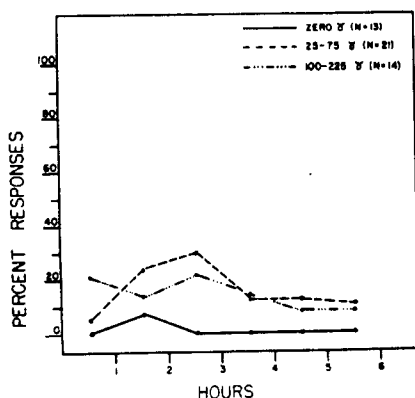
Item 5: "Is salivation decreased?" Here the peak was reached at $1\frac{1}{2}$



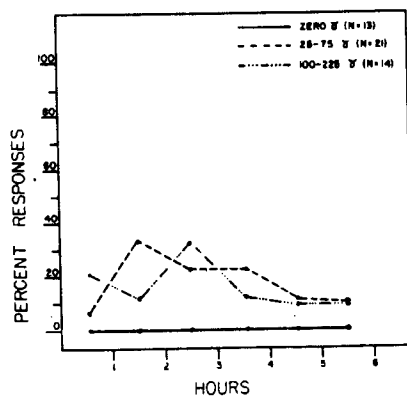
9. DO YOU HAVE A FUNNY TASTE IN YOUR MOUTH?



10. DO YOU HAVE A BITTER TASTE IN YOUR MOUTH?



11. ARE YOUR LIPS NUMB?

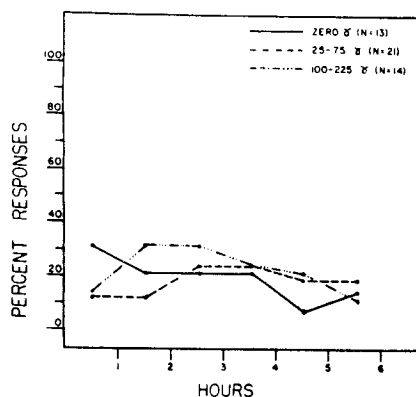


12. ARE YOUR LIPS DRAWN BACK AS IF YOU WERE SMILING?

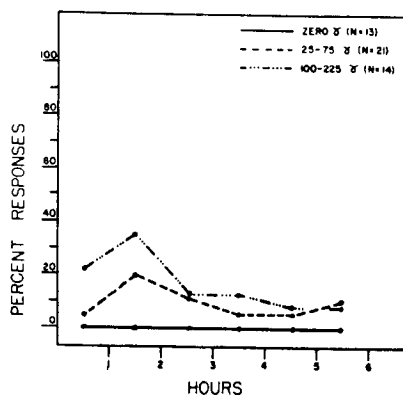
FIGURE 1 (continued)

hours for those receiving no LSD-25, when 23 per cent reported that their salivation was decreased. For those receiving a low dosage the peak was reached 3½ hours after the drug when 24 per cent reported that their salivation was decreased. About 36 per cent receiving the high dosage reported that their salivation was decreased in both the second and third intervals.

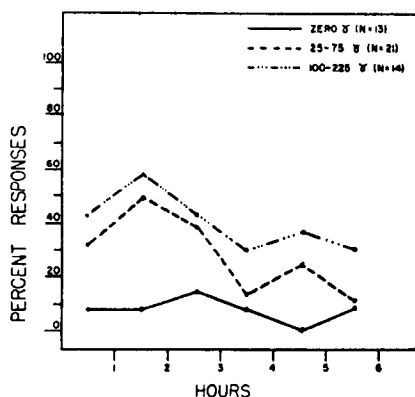
Item 6: "Is your appetite increased?" It should be noted that the subjects were fed about one-half hour after they took the drug, or just before the first question period. However, they were always instructed to give a positive response only if hunger was increased abnormally. Fifteen per cent of the subjects given no drug reported that their appetites were increased



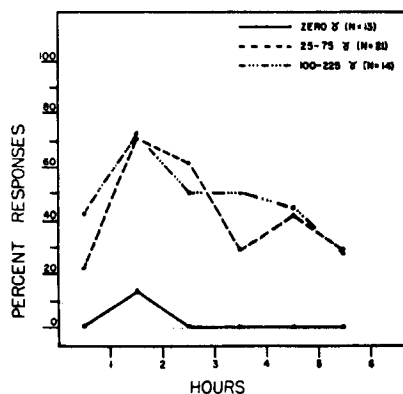
13. DOES YOUR HEAD ACHE?



14. ARE THINGS MOVING AROUND YOU?



15. DO YOU FEEL DIZZY?



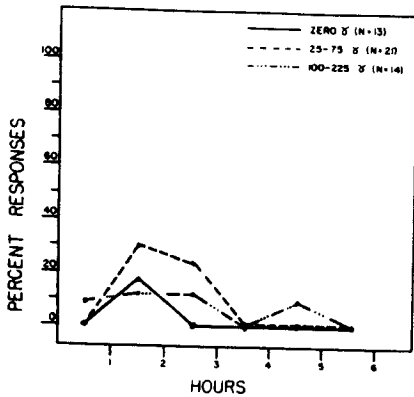
16. DO YOU FEEL UNSTEADY?

FIGURE 1 (continued)

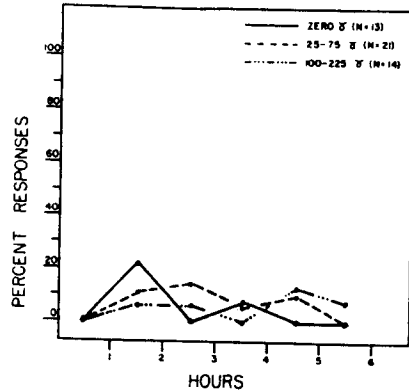
in the second period and about 19 per cent of the subjects receiving a low dose reported an increased appetite from 1½ to 3½ hours after the drug. Twenty-nine per cent of the subjects receiving the high dose reported that their appetites were increased in the third period, the peak for the large dose.

Item 7: "Is your appetite decreased?" About 23 per cent of the subjects receiving the placebo reported that appetite decreased after 3½ hours. At 1½ hours, nearly 38 per cent of the subjects receiving the low dose reported a decrease in appetite. Approximately 36 per cent of the subjects receiving 100-225 micrograms of the drug reported a decrease 1½ hours later.

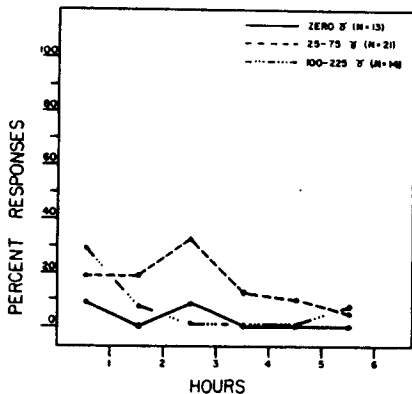
Item 8: "Do you have a dry taste in your mouth?" About 15 per cent



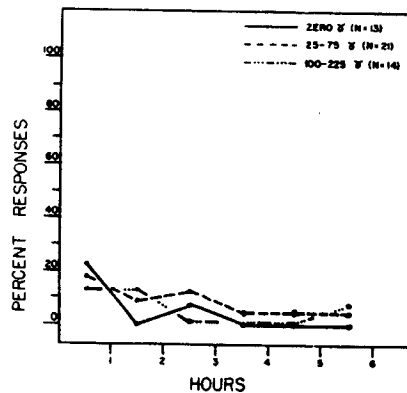
17. IS THERE DIFFICULTY IN BREATHING?



18. DO YOU PASS MORE URINE THAN USUAL?



19. ARE YOU AWARE OF YOUR HEART BEAT?



20. IS YOUR HEART BEAT FASTER THAN USUAL?

FIGURE 1 (continued)

of the persons receiving zero dosage reported in the first interval that they had a dry taste in their mouth. This percentage declined to zero by the fourth hour. On the other hand, the fourth hour was the peak hour for the low dosage group, when approximately 33 per cent of the group responded positively. The high dosage group never yielded a peak hour, and only about 21 per cent of the group reported a dry taste in the first and sixth hours.

Item 9: "Do you have a funny taste in your mouth?" Fifteen per cent of those receiving no LSD-25 reported that they had a funny taste in their mouth, whereas nearly 29 per cent of those receiving the low dose reported a funny taste at 1½ and 2½ hours. Fewer of those receiving the high dosage

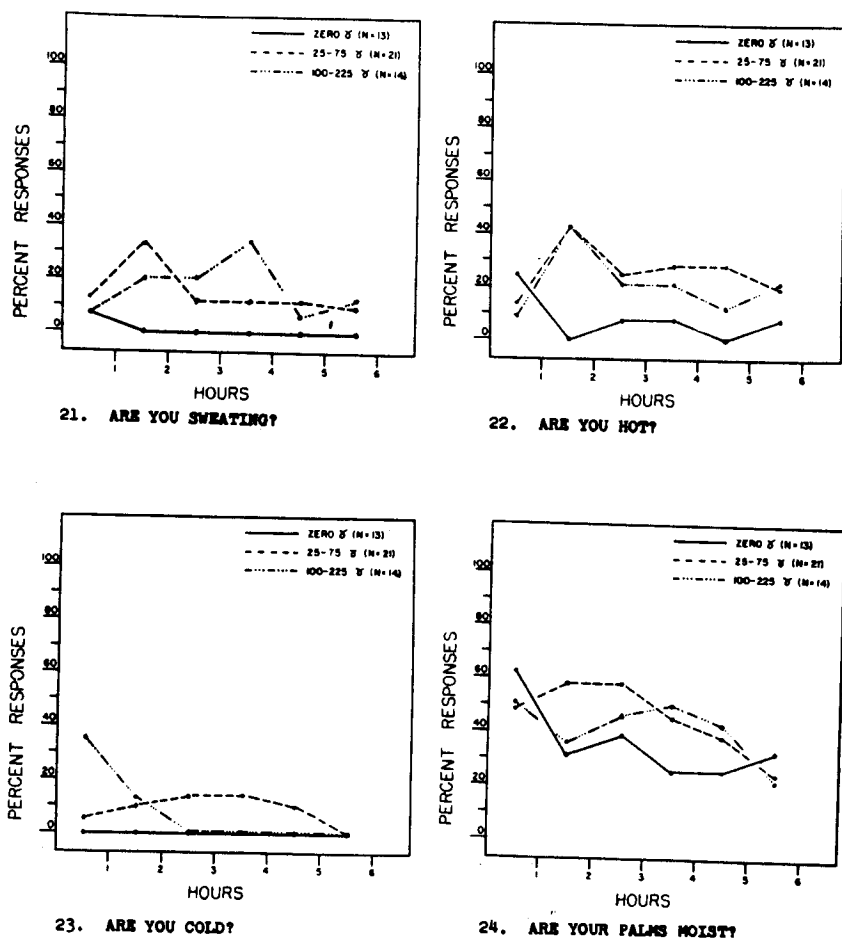
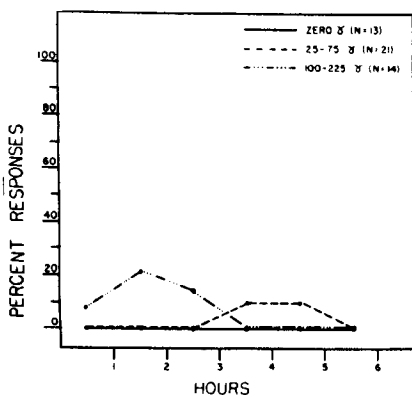


FIGURE 1 (continued)

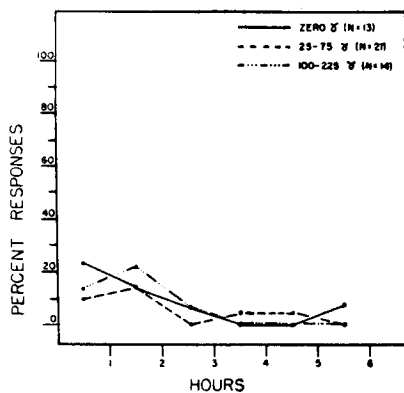
tended to report a funny taste in their mouth, in the same way that fewer tended to report a dry taste in their mouth. The peak with high dosage was again in the first half hour, when a little less than 29 per cent reported a funny taste, with the percentage declining as time progressed.

Item 10: "Is it a bitter taste?" Few in any of the groups responded positively to this question. Eight per cent of those receiving no LSD-25 responded positively and 14 per cent of those receiving a low dose responded positively 1½ hours later. The second period was the peak hour for the high dose when 21 per cent responded positively.

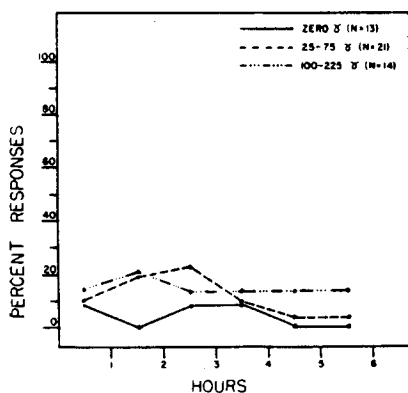
Item 11: "Are your lips numb?" Only 8 per cent of those receiving



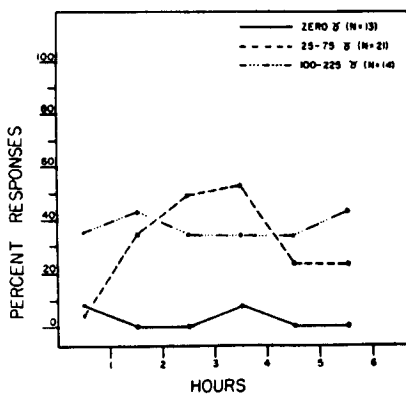
25. ARE YOUR PALMS DRY?



26. ARE YOUR PALMS COLD?



27. IS YOUR SKIN SENSITIVE?



28. DO YOU HAVE FUNNY FEELINGS ON YOUR SKIN?

FIGURE 1 (continued)

zero dosage reported that lips were numb in the second period, with no response in any other period. The low dosage group reached its peak at 2½ hours when 29 per cent gave a positive response. The high dosage group began at the peak with 28 per cent, then gradually declined until the sixth hour when only 14 per cent gave positive responses.

Item 12: "Are your lips drawn back as if smiling?" In this item not one of the subjects in the zero dose group gave a positive response at any hour. Among the subjects receiving the low dose, 33 per cent responded positively at 1½ hours which was the peak hour. For the high dosage group, 21 per cent responded positively in the first and third periods.

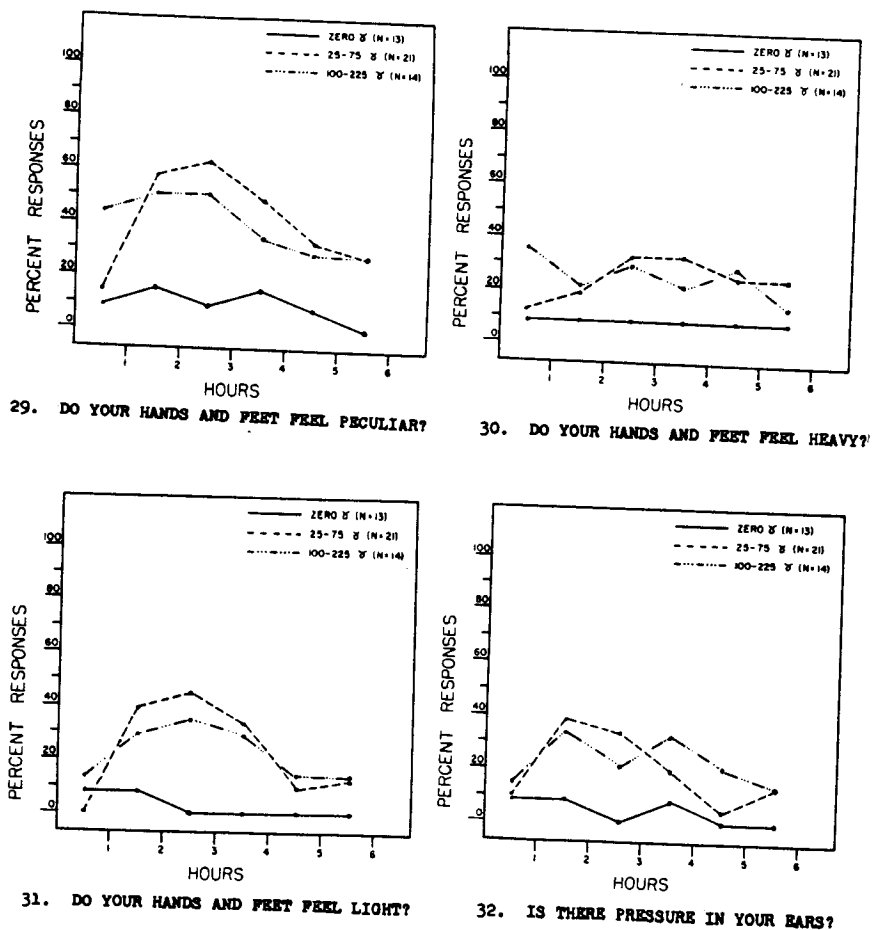
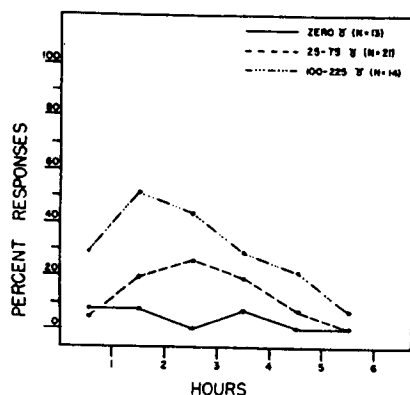


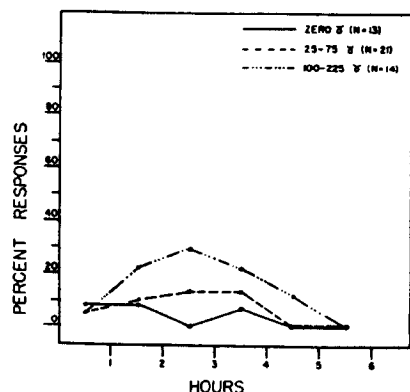
FIGURE 1 (continued)

Item 13: "Does your head ache?" A number of the subjects reported headaches whether they got the drug or not. Thirty-one per cent of the subjects who received no LSD-25 reported a headache $\frac{1}{2}$ hour after the placebo. Twenty-four per cent of the 25-75 microgram group reported a headache at the $2\frac{1}{2}$ and $3\frac{1}{2}$ hour intervals. Twenty-nine per cent of the high dosage group reported a headache at $2\frac{1}{2}$ hours.

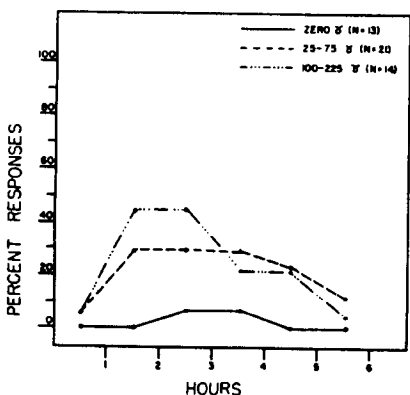
Item 14: "Are things moving around you?" None of the subjects who received no LSD-25 reported that things were moving around them. But among those who did receive LSD-25, 19 per cent of the low dosage group



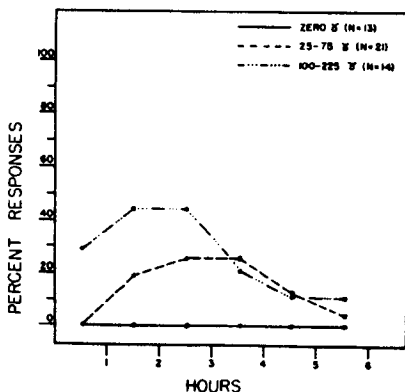
33. IS YOUR HEARING ABNORMAL?



34. IS YOUR HEARING MORE ACUTE THAN USUAL?



35. IS YOUR EYESIGHT BLURRED?



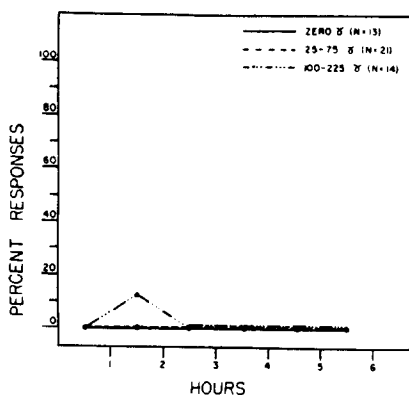
36. DO YOU HAVE DIFFICULTY IN FOCUSING YOUR VISION?

FIGURE 1 (continued)

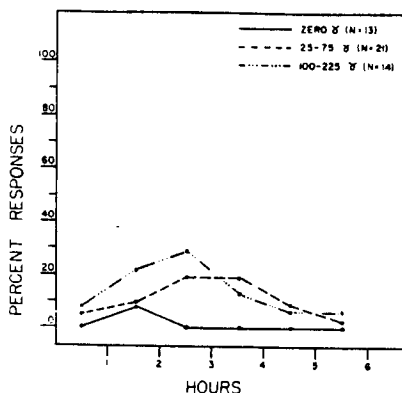
and 36 per cent of the high dosage group answered "yes" 1½ hours after the drug.

Item 15: "Do you feel dizzy?" Fifteen per cent of the subjects receiving no LSD-25 felt dizzy in the third period. Of those who received a low dose, 48 per cent reported feeling dizzy in the second period. In the sixth period there were 14 per cent who felt dizzy. Of those receiving the high dose, 57 per cent reported that they felt dizzy in the second interval.

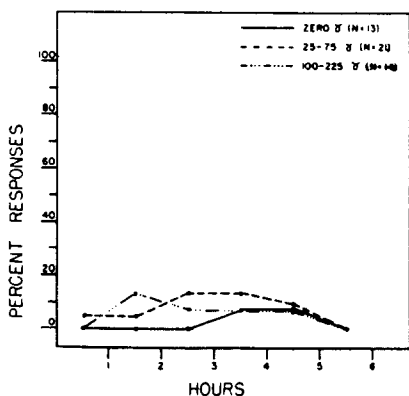
Item 16: "Do you feel unsteady?" Fifteen per cent of the subjects receiving the placebo reported that they felt unsteady 1½ hours later, whereas of those receiving the low dosage 71 per cent responded positively at 1½



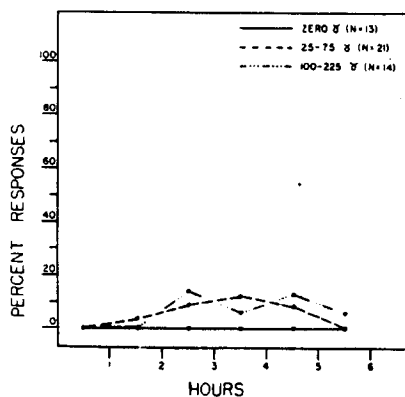
37. DO YOU SEE DOUBLE?



38. ARE SHAPES AND COLORS ALTERED IN ANY WAY?



39. DOES LIGHT BOTHER YOU?



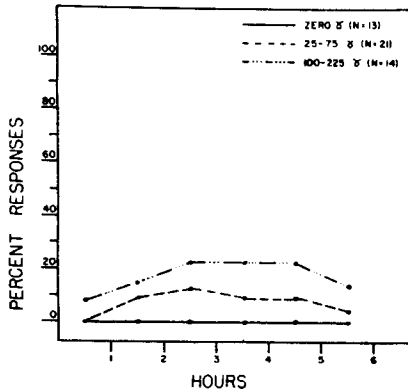
40. DO THINGS SEEM TOO CLOSE?

FIGURE 1 (continued)

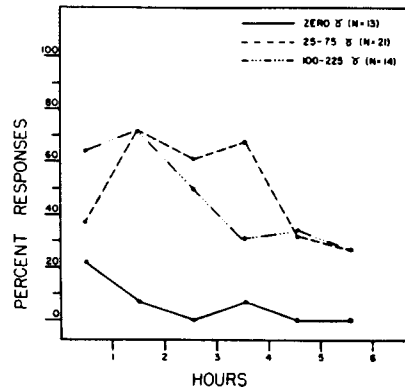
hours. For the high dosage, 71 per cent reported feeling unsteady 1½ hours after the drug.

Item 17: "Is there difficulty in breathing?" Only 8 per cent of the subjects receiving the zero dosage reported difficulty in breathing. In the second period, 29 per cent of the subjects receiving the low dose reported difficulty in breathing, and 14 per cent of the subjects receiving the high dosage reported this feeling. In this item, the highest peak was seen with the low doses.

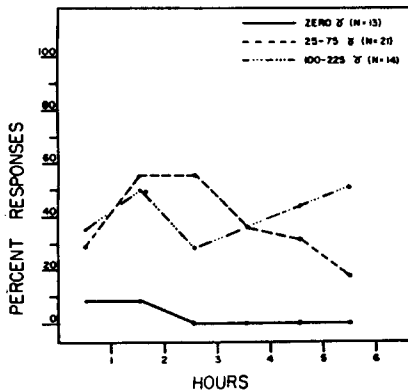
Item 18: "Do you pass more urine than usual?" Twenty-three per cent of the subjects who received a placebo said that they were passing more urine



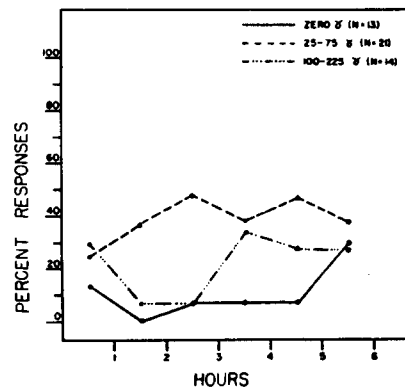
41. DO THINGS SEEM TOO FAR AWAY?



42. DO YOU TREMBLE INSIDE?



43. DO YOU FEEL WEAK?

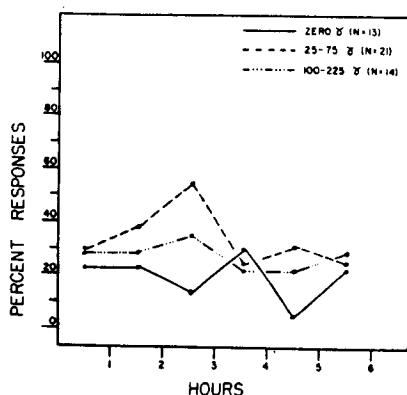


44. DO YOU FEEL FATIGUED?

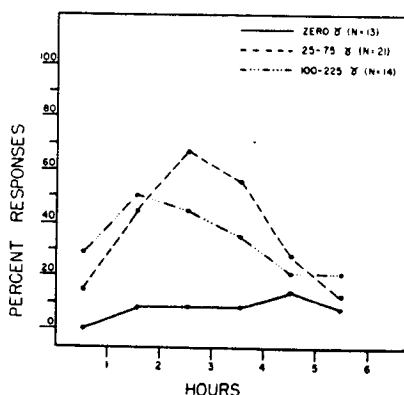
FIGURE 1 (continued)

than usual in the second period, and 14 per cent of those in the low dose group responded positively in the third interval. Seven per cent of the subjects who received the high dosage said that they were passing more urine than usual in the fifth interval.

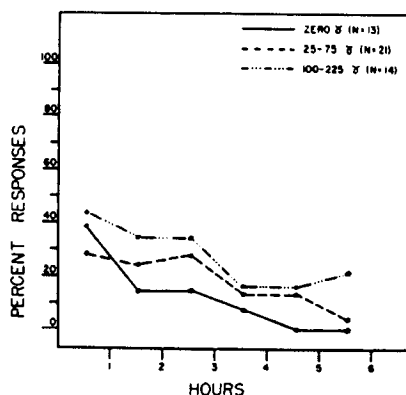
Item 19: "Are you aware of your heartbeat?" Only 8 per cent of the subjects who received no LSD-25 responded positively in the first and third periods. Of the subjects who received the low dose, 32 per cent reported that they felt their heartbeat in the third period, which was the peak hour. Of those in the 100-225 microgram group, 29 per cent said that they felt



45. DO YOU FEEL DROWSY?



46. DO YOU FEEL AS IF IN A DREAM?



47. ARE YOU ANXIOUS?

FIGURE 1 (continued)

their heartbeat in the first period. This effect declined rather rapidly, thereafter.

Item 20: "Is your heartbeat faster than usual?" Twenty-three per cent of the subjects who received no LSD-25 claimed that their heart rate was faster than usual during the first period. Nineteen per cent of the subjects who received the low dose said their heart rate was faster than usual. Fourteen per cent of the subjects who received the high dose experienced tachycardia at $\frac{1}{2}$ hour.

Item 21: "Are you sweating?" Eight per cent of the subjects who received the placebo said they were sweating in the first period, and never did thereafter. Of the subjects who received a low dose, 33 per cent said that they were sweating in the second period, which was the peak hour. Among the subjects who received the high dose, 36 per cent reported sweating in the fourth period, which was the peak.

Item 22: "Are you hot?" Although the room was warm (about 80° F) only 23 per cent of those receiving no LSD-25 said that they were hot, $\frac{1}{2}$ hour after the placebo. Forty-three per cent of the subjects who received a low dose reported feeling hot $1\frac{1}{2}$ hours later, and 43 per cent of those in the high dosage group responded positively at $1\frac{1}{2}$ hours.

Item 23: "Are you cold?" Although the room was somewhat warm, some of the subjects who received LSD-25 did say that they felt cold. None of the subjects who did not receive LSD-25 felt cold. In the low dosage group, 14 per cent said that they felt cold in the third and fourth periods. In the high dosage group, 36 per cent said that they felt cold in the first period, and this dropped down rapidly.

Item 24: "Are your palms moist?" Many of the subjects who did not receive LSD-25 reported moist palms. In the first $\frac{1}{2}$ hour, 62 per cent responded positively. The percentage who said that their palms were moist was never less than 24 per cent, and this per cent was not reached until $3\frac{1}{2}$ hours after the placebo. Of the people who received the low dose, 57 per cent said their palms were moist, $1\frac{1}{2}$ and $2\frac{1}{2}$ hours later. Among those in the high dose group, 50 per cent reported moist palms at the first $\frac{1}{2}$ hour.

Item 25: "Are your palms dry?" Few reported dry palms, but those who did always had received LSD-25; no one in the zero dose group did so. Of the people receiving the low dose, 14 per cent said that their palms were dry in the fourth and fifth periods while 21 per cent of the 100-225 microgram group said that their palms were dry in the second period.

Item 26: "Are your palms cold?" Of those receiving the placebo, 23 per cent reported that their palms were cold. Among the low dose group, 14 per

cent reported cold palms $1\frac{1}{2}$ hours after the drug. Twenty-one per cent of those receiving the high dosage reported cold palms $2\frac{1}{2}$ hours later.

Item 27: "Is your skin sensitive?" Eight per cent of the subjects who received zero dosage said that their skin was sensitive. Of those receiving the low dosage 24 per cent said that their skin was sensitive in the third period, and 21 per cent of the people receiving the high dosage responded positively to this item in the second period.

Item 28: "Do you have funny feelings on your skin?" Eight per cent responded positively with zero dosage. However, for the group receiving the low dosage, in the fourth period 52 per cent responded positively. In the group receiving the high dosage, 43 per cent responded positively, in the second period. The level remained high for both groups receiving LSD-25.

Item 29: "Do your hands and feet feel peculiar?" After the placebo fifteen per cent reported that their hands and feet felt peculiar in the second and the fourth periods. But 62 per cent of those who received a low dose reported that their hands and feet felt peculiar at the third interval; the level was always relatively high in all hours. For the high dose, 50 per cent reported that their hands and feet felt peculiar in the second and third intervals.

Item 30: "Do they feel heavy?" Eight per cent of those receiving the placebo answered positively in all hours. Thirty-three per cent of those receiving the low dose answered positively $2\frac{1}{2}$ and $3\frac{1}{2}$ hours later, and 36 per cent of those receiving the high dose reported heavy hands and feet $\frac{1}{2}$ hour after the drug.

Item 31: "Do they feel light?" Eight per cent who received zero LSD-25 answered this question positively in the first and second periods, whereas of those receiving the low dose, 43 per cent answered the question positively in the third period. Among the high dosage group, 36 per cent reported a feeling of lightness in the hands and feet during the third period.

Item 32: "Is there pressure in your ears?" Only 8 per cent of those receiving zero dosage reported pressure in their ears. Thirty-eight per cent of those receiving the low dosage responded positively, $1\frac{1}{2}$ hours later. Thirty-six per cent of those receiving the high dosage gave positive answers, with peaks $1\frac{1}{2}$ and $3\frac{1}{2}$ hours later.

Item 33: "Is your hearing abnormal?" Only 8 per cent of those receiving zero dosage gave positive responses to this item, whereas 24 per cent of those receiving a 25-75 microgram dose of the drug reported abnormal hearing in the third period. Fifty per cent of those receiving the high dosage gave positive answers in the second hour.

Item 34: "Is your hearing more acute than usual?" Eight per cent of the subjects in the placebo group responded positively, and 14 per cent of those

receiving a low dosage reported more acute hearing in the third and fourth periods. Twenty-nine per cent of those in the high dose group responded positively in the third period.

Item 35: "Is your eyesight blurred?" Eight per cent of the subjects receiving only water said that their eyesight was blurred $2\frac{1}{2}$ and $3\frac{1}{2}$ hours later, whereas 29 per cent of those receiving the low dose claimed that their eyesight was blurred from $1\frac{1}{2}$ to $3\frac{1}{2}$ hours. Forty-three per cent of those receiving the high dosage said that their eyesight was blurred from $1\frac{1}{2}$ to $2\frac{1}{2}$ hours later.

Item 36: "Do you have difficulty in focusing your vision?" None of the subjects receiving no LSD-25 responded positively to this item. However, 24 per cent of those receiving the low dosage claimed that they had difficulty focusing in the third and fourth periods. Forty-three per cent of those receiving 100-225 micrograms of LSD-25 had difficulty in focusing their vision in the second and third intervals.

Item 37: "Do you see double?" Practically no one saw double. None in the zero dosage and the 25-75 microgram group reported seeing double. Only 14 per cent of those who received a high dosage complained of seeing double, and this was $1\frac{1}{2}$ hours after the drug.

Item 38: "Are shapes and colors altered in any way?" Eighteen per cent of the people receiving zero dose said that the shapes and colors were altered during the second period. Nineteen per cent of those receiving a low dose felt that shapes and colors were altered during the third and fourth periods. Twenty-nine per cent of those receiving the high dosage reported that shapes and colors were altered, primarily in the third interval.

Item 39: "Does light bother you?" Only 8 per cent of the placebo group responded positively to this question, $3\frac{1}{2}$ and $4\frac{1}{2}$ hours after the water. Fourteen per cent of those receiving a low dose felt that light bothered them $2\frac{1}{2}$ and $3\frac{1}{2}$ hours later, while 14 per cent of those in the high dosage group stated that light bothered them at $1\frac{1}{2}$ hours.

Item 40: "Do things seem too close?" No one receiving the zero dosage claimed things seemed too close. Fourteen per cent receiving a low dose complained that things seemed too close in the fourth period. Fourteen per cent of those receiving the high dosage said that things seemed too close in the third and fifth periods.

Item 41: "Do things seem too far away?" Those receiving zero dosage always answered negatively. In the third period, 14 per cent of the people receiving a low dosage felt that things seemed too far away. Twenty-one per cent of those receiving a high dosage reported that things seemed too far away in the third, fourth, and fifth periods.

Item 42: "Do you tremble inside?" One-half hour after taking the placebo 23 per cent of the people said that they trembled inside, but this rapidly fell off to 8 per cent or less in the succeeding hours. On the other hand, for those who took the drug, 71 per cent of those receiving the low dose and 71 per cent of those who took the high dose complained of inner trembling 1½ hours later.

Item 43: "Do you feel weak?" Only 8 per cent of the people receiving no LSD-25 felt weak in the first 1½ hours, whereas 57 per cent of those receiving the low dosage felt weak 1½ and 2½ hours later. Half of those receiving a high dosage felt weak at 1½ and 5½ hours.

Item 44: "Do you feel fatigued?" The number of positive responses to this item went up toward the end of the experiment. For those subjects who received zero dosage, it went up as high as 31 per cent in the sixth period. Forty-eight per cent reported it in the third and fifth periods (low dosage). On the other hand, among those receiving 100-225 gamma, the percentage giving positive responses was only 36 in the fourth period.

Item 45: "Do you feel drowsy?" Thirty-one per cent receiving a placebo felt drowsy in the fourth interval. Fifty-seven per cent of the subjects receiving the low dosage of LSD-25 felt drowsy in the third period, and 36 per cent of those in the high dosage group felt drowsy in the third period.

Item 46: "Do you feel as if in a dream?" Fifteen per cent of the subjects receiving zero dose felt as though they were in a dream 4½ hours later. The subjects receiving a 25-75 microgram dose of LSD-25 felt as if in a dream mainly at 2½ hours, when 67 per cent of them answered "Yes" to this question. Those in the high dosage group reached their peak at 1½ hours, when 50 per cent of them reported experiencing a dream-like state.

Item 47: "Are you anxious?" For all subjects, whether or not they received LSD-25, the total number of responses was highest in the first period, and declined thereafter. Thirty-eight per cent of the subjects who received a placebo reported anxiety in the first period. By the fifth period, no one reported it. For those receiving a low dose, 29 per cent responded positively in the first period, declining to 4 per cent in the sixth period. Among those in the high dose group, 43 per cent stated that they were anxious in the first period, and by the fourth and fifth periods, only 14 per cent reported it.

Average percentage positive responses to 47 questions (Figure 2). When responses to all items for the zero dose group are combined, there is at first a linear decrease with time in percentage of responses with the exception of a slight peak at 3½ hours. Compare this with the curve for the low dose group. Following an initially low level of responses there is a sharp rise to a maximum at 2½ hours. There is then a gradual decline.

The high dosage curve begins at a relatively high level in the first $\frac{1}{2}$ hour; it reaches its peak, which is higher than that of the low dose, at $1\frac{1}{2}$ hours. Gradual decline follows.

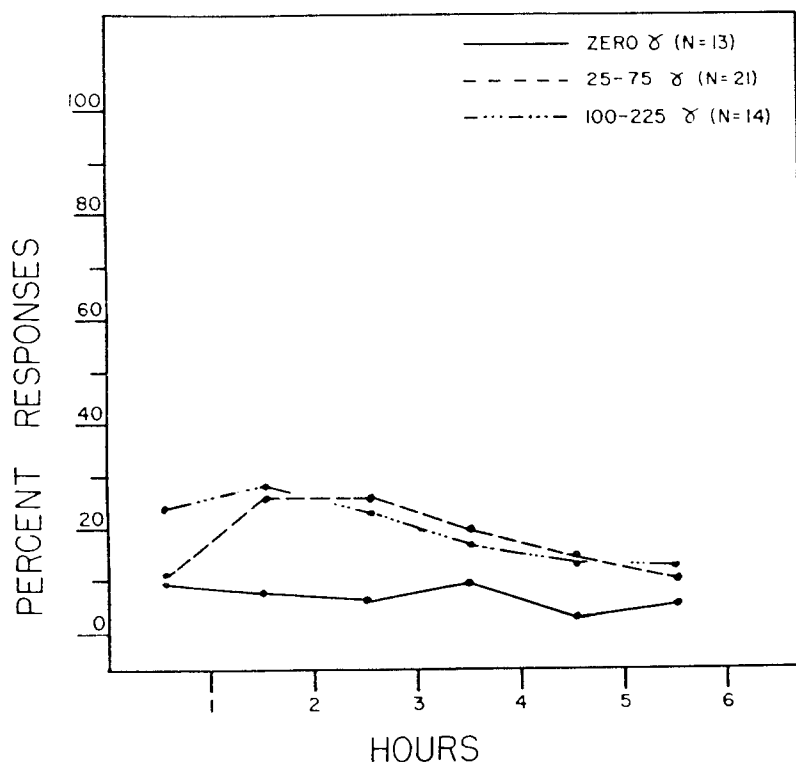


FIGURE 2
AVERAGE PERCENT POSITIVE RESPONSE TO 47 QUESTIONS

(3). *Discussion.* The symptoms which seem most closely related to the drugs, by virtue of their receiving considerably larger responses by the drug groups than by the placebo group, are the following: things seeming to move around subjects, dizziness, unsteadiness, sweating, feeling hot or cold, paraesthesias, peculiar feeling of limbs, heaviness or lightness of limbs, pressure in ears, blurred eyesight, difficulty in focusing vision, inner trembling, weakness and dream-like feeling.

Some items differentiated between the placebo group and the drug group to a lesser extent. These symptoms are: choking, changes in appetite, dry and funny taste in mouth, numbness of lips, lips drawn back as if smiling, aware-

ness of heartbeat, hyperacusia, alteration of shapes and colors, and objects appearing too far away. Illness, nausea, decreased salivation, and abnormal hearing did not seem to occur frequently until higher doses of the drug were taken.

In addition to symptoms which seem to be drug-produced, other differences appear among the three groups. As a whole, most of the responses by the group taking zero dosage are given $\frac{1}{2}$ hour after taking the placebo and taper off quickly. Under the low doses of LSD-25, symptoms generally attain a peak between $1\frac{1}{2}$ and $2\frac{1}{2}$ hours after the drug. They then decline gradually and are often still reported by the last hour. Higher doses seem to take effect much more rapidly, and the peak is usually reached at $1\frac{1}{2}$ hours. The decline is much more gradual than under the low dose and the level of response is usually higher throughout.

If the three groups of subjects were correlated, more accurate results would be obtained since individual variability would be controlled. However, these results do give some indication of LSD-25 symptomatology.

One other weakness must be pointed out: in the case of symptoms reported frequently by all three groups there is no way of knowing whether the feelings experienced are subjectively the same or whether the drug actually does produce different qualitative results in areas receiving the same positive responses. The questionnaire is not sufficiently definitive for this, and it is difficult to construct one which does measure qualitative differences in such terms as "Do you feel drowsy?" or "Does your head ache?"

b. Average percentage response per hour.

(1). *Statistical procedure.* The total number of plus (or positive) responses made by each group to each question throughout the six-interval day was counted by the IBM 101 Electronic Statistical Machine. The average percentage responding per hour was then determined by means of the following formula:

$$M_{\%} = \frac{\Sigma +}{6N} \times 100 \quad (2)$$

where $M_{\%}$ equals the average percentage responding positively per hour, $\Sigma +$ equals the sum of plus responses throughout six intervals, and N equals the number of subjects.

The groups are the same as those described in the previous section on hourly percentage responses to questions. The number of subjects equals 13, 21, and

14 for the zero, 25-75 micrograms, and 100-225 microgram groups, respectively.

(2). *Results.* It can be seen from Table 2 that in 26 of the 47 questions, increasing percentages of responses are made under increasing dosages of the drug. These questions are: (1) "Do you feel ill in any way?", (2) "Are you nauseated?", (3) "Have you a feeling of choking?", (5) "Is salivation decreased?", (6) "Is your appetite increased?", (7) "Is your appetite decreased?", (10) "Is it (the funny taste) a bitter taste?", (11) "Are your lips numb?", (14) "Are things moving around you?", (15) "Do you feel dizzy?", (16) "Or (do you feel) unsteady?", (21) "Are you sweating?", (25) "Are your palms dry?", (27) "Is your skin sensitive?", (28) "Do you have funny feelings on your skin?", (30) "Do they (your hands and feet) feel heavy?", (31) "Or (do they feel) light?", (32) "Is there pressure in your ears?", (34) "Is it (your hearing) more acute than usual?", (35) "Is your eyesight blurred?", (36) "Do you have difficulty in focusing your vision?", (38) "Are shapes and colors altered in any way?", (41) "Or (do things seem) too far away?", (42) "Do you tremble inside?", (43) "Do you feel weak?", and (47) "Are you anxious?".

In 17 questions the highest percentage of response occurs at intermediate doses of LSD-25. Among these are: (4) "Is salivation increased?", (8) "Do you have a dry taste in your mouth?", (12) "Are your lips drawn back as if you were smiling?", (13) "Does your head ache?", (17) "Is there difficulty in breathing?", (18) "Do you pass more urine than usual?", (19) "Are you aware of your heartbeat?", (20) "Is it faster than usual?", (22) "Are you hot?", (23) "Or (are you) cold?", (24) "Are your palms moist?", (29) "Do your hands and feet feel peculiar?", (33) "Is your hearing abnormal?", (39) "Does light bother you?", (44) "Or (do you feel) fatigued?", (45) "Do you feel drowsy?", and (46) "Do you feel as if in a dream?".

Some of the differences between percentages of the different groups responding are relatively small and others are large. Whether these differences are real differences or whether they are a result of chance cannot be determined by inspection. Results of statistical treatment of the differences are shown in Tables 8-10.

Equal percentages of positive responses were made by the two drug groups to the questions: (9) "Do you have a funny taste in your mouth?", (40) "Do things seem too close?", and (26) "Or (are your palms) cold?", with a larger per cent responding under zero than under the drug in the case of the latter question only. (37) "Do you see double?", received equal response by the zero group and the 25-75 gamma group, with a slightly larger per cent responding under the high dose.

Under zero dosage, (24) "Are your palms moist?", received approximately one-third positive responses per hour, while (45) "Are you drowsy?" was positively responded to by about one-fourth of the group. Twenty per cent reported a headache, 13 per cent anxiety and 11 per cent stated they felt decreased appetite and fatigue. Less than 10 per cent of the subjects responded positively to all the other items. These findings are more readily seen in Table 3

There were eight items to which none of the subjects receiving no LSD-25 responded positively (see Table 3). These were: (12) "Are your lips drawn back as if you were smiling?", (14) "Are things moving around you?", (23) "Are you cold?", (25) "Are your palms dry?", (36) "Do you have difficulty in focusing your vision?", (37) "Do you see double?", (40) "Do things seem too close?", and (41) "Do things seem too far away?".

Table 4

While only one item received over 30 per cent average hourly response by the zero dose group, nine were responded to at this frequency by subjects under 25-75 micrograms of the drug (see Table 4). These included: (24) "Are your palms moist?", (16) "Do you feel unsteady?", (29) "Do your hands and feet feel peculiar?", (42) "Do you tremble inside?", (43) "Do you feel weak?", (44) "Do you feel fatigued?", (46) "Do you feel as if in a dream?", (45) "Do you feel drowsy?", and (28) "Do you have funny feelings on your skin?".

Thirteen symptoms were reported by no more than 10 per cent of the low dose group (see Table 4): faster heartbeat, things moving around, difficulty in breathing, coldness, photophobia, things "seeming too far away, bitter taste in mouth, polyuria, cold palms, hyperacusia, things seeming too close, dry palms, and double vision. Items are listed in order of decreasing frequency and only the last symptom had no response at all under this dose of drug.

When subjects received 100-225 micrograms of LSD-25 the item to which they responded positively most frequently (see Table 5) was (16) "Do you feel unsteady?" Nearly half of the subjects in this dosage range gave positive responses to this item. Almost as many responded positively to (42) "Do you tremble inside?" At this dosage there were also nine questions to which more than 30 per cent of the subjects responded positively. Of these nine questions to which more than 30 per cent of the group receiving the high dosage responded positively, seven were also the same questions that more than 30 per cent of the group receiving the low dosage responded positively. The only two items which were different, and which therefore had moved up in percentage of response were: (15) "Do you feel dizzy?", to which 40 per cent of the subjects receiving the high dosage responded positively, (whereas only 29

TABLE 3

AVERAGE PERCENT RESPONDING POSITIVELY UNDER ZERO LSD-25
 (Questions are ranked from highest percent (rank 1) of subjects responding
 positively to lowest percent. N = 13)

Rank	Percent responding	Question number	Question
1	35	24	Are your palms moist?
2	24	45	Do you feel drowsy?
3	20	13	Does your head ache?
4	13	47	Are you anxious?
5.5	11	7	Is your appetite decreased?
5.5	11	44	Do you feel fatigued?
8	9	4	Is salivation increased?
8	9	26	Are your palms cold?
8	9	29	Do your hands and feet feel peculiar?
10.5	8	1	Do you feel ill in any way?
10.5	8	9	Do you have a funny taste in your mouth?
13	7	15	Do you feel dizzy?
13	7	22	Are you hot?
13	7	30	Do your hands and feet feel heavy?
16	6	5	Is salivation increased?
16	6	42	Do you tremble inside?
16	6	46	Do you feel as if in a dream?
19.5	5	6	Is your appetite increased?
19.5	5	8	Do you have a dry taste in your mouth?
19.5	5	18	Do you pass more urine than usual?
19.5	5	20	Is your heart beat faster than usual?
24	4	10	Do you have a bitter taste in your mouth?
24	4	27	Is your skin sensitive?
24	4	32	Is there pressure in your ears?
24	4	33	Is your hearing abnormal?
24	4	34	Is it more acute than usual?
28	3	2	Are you nauseated?
28	3	16	Do you feel unsteady?
28	3	17	Is there difficulty in breathing?
32.5	2	19	Are you aware of your heart beat?
32.5	2	28	Do you have funny feelings on your skin?
32.5	2	31	Do your hands and feet feel light?
32.5	2	35	Is your eyesight blurred?
32.5	2	39	Does light bother you?
32.5	2	43	Do you feel weak?
37.5	1	3	Have you a feeling of choking?
37.5	1	11	Are your lips numb?
37.5	1	21	Are you sweating?
37.5	1	38	Are shapes and colors altered in any way?
43.5	0	12	Are your lips drawn back as if you were smiling?
43.5	0	14	Are things moving around you?
43.5	0	23	Are you cold?
43.5	0	25	Are your palms dry?
43.5	0	36	Do you have difficulty in focusing your vision?
43.5	0	37	Do you see double?
43.5	0	40	Do things seem too close?
43.5	0	41	Do things seem too far away?

TABLE 4
AVERAGE PERCENT RESPONDING POSITIVELY UNDER 25-75 GAMMA LSD-25
(Questions are ranked from highest percent (rank 1) of subjects responding positively to lowest percent. N = 21)

Rank	Percent of subjects responding positively	Question number	Question
1	45	24	Are your palms moist?
2	43	16	Do you feel unsteady?
3	41	29	Do your hands and feet feel peculiar?
4	40	42	Do you tremble inside?
5.5	39	43	Do you feel weak?
5.5	39	44	Do you feel fatigued?
7	37	46	Do you feel as if in a dream?
8	34	45	Do you feel drowsy?
9	31	28	Do you have funny feelings on your skin?
10	29	15	Do you feel dizzy?
11	27	13	Does your head ache?
12	26	22	Are you hot?
13	25	30	Do your hands and feet feel heavy?
14	23	31	Do your hands and feet feel light?
15.5	22	35	Is your eyesight blurred?
15.5	22	47	Are you anxious?
17	20	32	Is there pressure in your ears?
18.5	19	9	Do you have a funny taste in your mouth?
18.5	19	12	Are your lips drawn back as if you were smiling?
21	17	8	Do you have a "dry" taste in your mouth?
21	17	19	Are you aware of your heart beat?
21	17	21	Are you sweating?
23	16	11	Are your lips numb?
24.5	15	2	Are you nauseated?
24.5	15	4	Is salivation increased?
26.5	14	7	Is your appetite decreased?
26.5	14	36	Do you have difficulty in focusing your vision?
28.5	12	5	Is salivation decreased?
28.5	12	33	Is your hearing abnormal?
32	11	1	Do you feel ill in any way?
32	11	3	Have you a feeling of choking?
32	11	6	Is your appetite increased?
32	11	27	Is your skin sensitive?
32	11	38	Are shapes and colors altered in any way?
35	10	20	Is your heart beat faster than usual?
37	9	14	Are things moving around you?
37	9	17	Is there difficulty in breathing?
37	9	23	Are you cold?
39.5	8	39	Does light bother you?
39.5	8	41	Do things seem too far away?
43	7	10	Do you have a bitter taste in your mouth?
43	7	18	Do you pass more urine than usual?
43	7	26	Are your palms cold?
43	7	34	Is your hearing more acute than usual?
43	7	40	Do things seem too close?
46	3	25	Are your palms dry?
47	0	37	Do you see double?

TABLE 5
PERCENT RESPONDING POSITIVELY UNDER 100-225 GAMMA LSD-25
(Questions ranked from highest percent (rank 1) of subjects responding to lowest percent. $N = 14$.)

Rank	Percent responding	Question number	Question
1	48	16	Do you feel unsteady?
2	47	42	Do you tremble inside?
3.5	41	24	Are your palms moist?
3.5	41	43	Do you feel weak?
5.5	40	15	Do you feel dizzy?
5.5	40	29	Do your hands and feet feel peculiar?
7	38	28	Do you have funny feelings on your skin?
8	33	46	Do you feel as if in a dream?
9	30	30	Do your hands and feet feel heavy?
10	28	45	Do you feel drowsy?
11.5	27	36	Do you have difficulty in focusing your vision?
11.5	27	47	Are you anxious?
13	26	2	Are you nauseated?
15	24	1	Do you feel ill in any way?
15	24	32	Is there pressure in your ears?
15	24	35	Is your eyesight blurred?
17.5	23	31	Do your hands and feet feel light?
17.5	23	44	Do you feel fatigued?
19	22	5	Is salivation decreased?
20.5	21	11	Are your lips numb?
20.5	21	22	Are you hot?
22	20	13	Does your head ache?
23.5	19	7	Is your appetite decreased?
23.5	19	9	Do you have a funny taste in your mouth?
25.5	18	21	Are you sweating?
25.5	18	27	Is your skin sensitive?
27.5	17	6	Is your appetite increased?
27.5	17	14	Are things moving around you?
29	16	8	Do you have a dry taste in your mouth?
30	15	34	Is your hearing more acute than usual?
31.5	14	12	Are your lips drawn back as if you were smiling?
31.5	14	38	Are shapes and colors altered in any way?
33	13	41	Do things seem too far away?
34	12	3	Have you a feeling of choking?
35	9	10	Do you have a bitter taste in your mouth?
36.5	8	20	Is your heart beat faster than usual?
36.5	8	23	Are you cold?
40	7	17	Is there difficulty in breathing?
40	7	19	Are you aware of your heart beat?
40	7	25	Are your palms dry?
40	7	26	Are your palms cold?
40	7	40	Do things seem too close?
44	6	4	Is salivation increased?
44	6	18	Do you pass more urine than usual?
44	6	39	Does light bother you?
46	3	33	Is your hearing abnormal?
47	2	37	Do you see double?

per cent of those receiving the low dosage did so), and (30) "Do your hands and feet feel heavy?", to which 30 per cent of the subjects responded positively with the high dosage, and 25 per cent of the subjects receiving the low dosage responded positively. Fatigue and drowsiness were less important to the high dosage group and fewer than 20 per cent reported these symptoms.

There were 13 items which received positive responses by no more than 10 per cent of the group (see Table 5). Of these 13 items, there were 9 items in common with the low dose group: (37) "Do you see double?", (39) "Does light bother you?", (18) "Do you pass more urine than usual?", (40) "Do things seem too close?", (26) "Are your palms cold?", (25) "Are your palms dry?", (17) "Is there difficulty in breathing?", (23) "Are you cold?", (10) "Do you have a bitter taste in your mouth?" These items were rarely responded to by subjects receiving LSD-25, regardless of dose.

While none of the questions received zero response from the 100-225 microgram group, the least important question was (37) "Do you see double?" to which an average of 2 per cent per hour responded positively.

(3). *Discussion.* Some of the most interesting data emanate from the zero dosage group. It is interesting that even in this group of individuals who received no LSD-25, but only a placebo consisting of a cup of water, 35 per cent of the responses to "Are your palms moist?" were positive. Several reasons for this large number of positive responses are suggested. First, it may be that individuals normally have moist palms but are not made aware of it until they are asked a direct question. Secondly, the subjects may have been anxious in the situation, and it is well known that anxiety causes moist palms due to perspiration. Although a good many of the sessions were held in a very warm room, the high incidence of moist palms cannot be attributed to this since only one per cent of the subjects responded that they were sweating, when they did not receive LSD-25. The group receiving the drug gave similar high percentage responses to this question and it appears that this symptom is independent of the drug action, but results from our test situation.

The next question to receive a large number of responses by the zero dose group was "Do you feel drowsy?". Twenty-four per cent of the responses were positive. Drowsiness is one of the symptoms which is most amenable to suggestion. The high incidence of drowsiness may also be due to the fact that subjects were situated in a very warm and restful atmosphere, and in addition they were probably fatigued by the rigorous series of tests to which they were submitted. Thirty-four per cent and 28 per cent of subjects in the low and high dose groups, respectively, also gave positive responses to this item showing that this question is not especially discriminatory. It is very likely that the reasons suggested for the high response under zero dosage are applicable to the

drug groups, as well. It is interesting that the highest percentage response occurred with the 25-75 microgram group. The significance of this observation is questionable, however, since the three dose groups were only partially correlated, and the samples were small. Small differences in percentages cannot be given too much significance because of the individual variability present.

The next most common symptom in zero dosage was headache. One out of five responses, on an average, was positive to this. Why there are so many positive responses is difficult to say. Interestingly enough, under 100-225 micrograms, there were 20 per cent giving positive responses to this item, and under 25-75 micrograms, 27 per cent gave positive responses. Regardless of whether the subject took LSD-25 or what the dosage was, about one-fifth of the subjects reported headache. This is not a discriminating question.

Question (47) "Are you anxious?" received positive responses by 13 per cent of the zero dose group; this was the fourth most frequently reported symptom with this dose. Larger percentages of the subjects taking the drug responded to this question indicating that the item probably significantly discriminates. Differences were not great, however, and reliability of the differences would have to be tested statistically. The stress situation of taking a new drug, and not knowing the effects it would have, seem to contribute to the positive responses made in this case.

Decreased appetite reported by zero dose subjects seems related to anxiety. Slightly greater percentages of the group under the effects of LSD-25 responded positively to this item, perhaps relating to the increased anxiety reported by these groups as compared to the placebo group.

Fatigue which was reported might be a result of the general situation of being tested all day. It is strange that the low dose group responded positively to a much greater extent than either of the other groups; it should be remembered, however, that subjects were not identical in each group.

Among the symptoms reported infrequently or never by the zero group, those which seem to have some relationship to LSD-25 were: difficulty in focusing vision, blurred eyesight, inner trembling, dream-like feeling, weakness, pressure in ears, funny feelings on the skin, peculiar feeling of limbs, heaviness and lightness of limbs, nausea, sweating, and feeling hot. Whether or not the differences in percentage response to these questions are significant will be shown in a later discussion.

The average hourly percentage response as a means of comparing the three groups is both advantageous and disadvantageous. Its advantage lies in the fact that there is one representative statistic for each group which can be compared with greater ease than six numbers representing six hours. There is a disadvantage, however, because a great deal of valuable information is

lost. If the reader knows only the average per cent response to each item there is a tendency to assume that shape of the time curve is similar for the three groups. That this is not so was shown in the graphs of each question. Frequently the maximum response under a placebo occurred in the first half-hour and then leveled off while for the drug group the peak usually appeared $1\frac{1}{2}$ to $2\frac{1}{2}$ hours after ingestion of the LSD-25. Consequently, some of the questions receiving a relatively low per cent response by zero dose subjects received initially high responses, but rapid leveling off reduced the the average hourly response considerably. It is still of value to compare the average responses, but the nature of the difference is more clearly understood through study of the responses at each hour.

On the basis of the average hourly percentage responses, it would appear that the characteristic feature of items which elicit positive responses under LSD-25, is that they are all related to autonomic functions, especially to autonomic functions which may be said to be elicited by anxiety. For example, the top items of the 25-75 microgram LSD-25 dosage involved such symptoms as moist palms, unsteadiness, peculiar feelings of hands and feet, inner trembling, and weakness. Similarly, with the high dosage of LSD-25 the symptoms which were most frequently elicited were unsteadiness, inner trembling, moist palms, weakness, dizziness, and peculiar feelings of hands and feet. By contrast, the most frequent symptoms of the zero dosage group were (aside from the moist palms) drowsiness, headache, anxiety, decreased appetite, and fatigue. These are mostly depressive symptoms as compared with the othosympathetic symptoms elicited by LSD-25. In a sense, the symptoms which appear under zero dosage might be related to those that are brought forth by cholinergic drugs (or histamines), whereas the symptoms elicited by LSD-25 mainly resemble those that are elicited by adrenergic drugs.

c. Ranks of questions.

(1). *Statistical procedure.* Questions were ranked within each of the three dose groups (zero, 25-75 micrograms and 100-225 micrograms of LSD-25), according to the average percentage responding per hour as indicated in Table 3. Rank "1" was delegated to that question having the greatest percentage response, rank "2" to that having the second highest percentage response, etc.

The relationship among rank positions of questions in the three groups of subjects was determined by applying equation (3) to the ranks comparing the three groups taken two at a time, (zero with 25-75 micrograms, zero with 100-225 micrograms, and 25-75 micrograms with 100-225 micrograms),

$$\rho = 1 - \frac{6\sum D^2}{N(N^2 - 1)} \quad (3)$$

where ρ equals the rank difference correlation coefficient, D equals the difference between the ranks of a question in two different dose groups, $\sum D^2$ equals the sum of the squared rank differences for all 47 items in the groups compared, and N equals the number of questions, 47. Statistical tables indicate minimum values for correlation coefficients to be accepted as significant at the .05 and .01 levels.

(2). *Results.* The questions are listed in their rank order and the average percentage response per hour is given for the zero dosage group, 25-75 microgram LSD-25 group and 100-225 microgram LSD-25 group in Tables 3, 4, and 5, respectively. In Table 6 the rank of each question within each of the three dose groups is given in order to enable comparison of the relative importance of the questions in the different groups.

Table 6

In the zero dosage group, the four highest ranking questions were (24) "Are your palms moist?", (45) "Do you feel drowsy?", (13) "Does your head ache?", and (47) "Are you anxious?". The lowest ranking items in this group to which no subject responded at any time were the following: (12) "Are your lips drawn back as if you were smiling?", (14) "Are things moving around you?", (23) "Are you cold?", (25) "Are your palms dry?", (36) "Do you have difficulty in focusing your vision?", (37) "Do you see double?", (40) "Do things seem too close?", and (41) "Do things seem too far away?".

In contrast to this, the four questions receiving highest percentage response by the low dose group were: (24) "Are your palms moist?", (16) "Do you feel unsteady?", (29) "Do your hands and feet feel peculiar?", and (42) "Do you tremble inside?", while those receiving the least response were: (10) "Do you have a bitter taste in your mouth?", (18) "Do you pass more urine than usual?", (26) "Are your palms cold?", (34) "Is your hearing more acute than usual?", (40) "Do things seem too close?", (24) "Are your palms dry?", and (37) "Do you see double?".

Among the high dose group, questions (16) "Do you feel unsteady?", (42) "Do you tremble inside?", (24) "Are your palms moist?", and (43) "Do you feel weak?" were most frequently responded to; the following items received the lowest average hourly percentage response: (4) "Is salivation increased?", (18) "Do you pass more urine than usual?", (39) "Does light bother you?", (33) "Is your hearing abnormal?", and (37) "Do you see double?".

TABLE 6
RANK OF EACH QUESTION FOR EACH OF THREE LSD-25 DOSAGE GROUPS
(Rank 1 indicates highest percent of positive responses. Succeeding numbers represent decreasing percents.)

Question number	Question	Rank of question		
		N = 13 0 Gamma	N = 21 25-75 Gamma	N = 14 100-225 Gamma
1	Do you feel ill in any way?	10.5	32	15
2	Are you nauseated?	28	24.5	13
3	Have you a feeling of choking?	37.5	32	34
4	Is salivation increased?	8	24.5	44
5	Or decreased?	16	28.5	19
6	Is your appetite increased?	19.5	32	27.5
7	Or decreased?	5.5	26.5	23.5
8	Do you have a "dry" taste in your mouth?	19.5	21	29
9	Do you have a funny taste in your mouth?	10.5	18.5	23.5
10	Is it a bitter taste?	24	43	35
11	Are your lips numb?	37.5	23	20.5
12	Or drawn back as if you were smiling?	43.5	18.5	31.5
13	Does your head ache?	3	11	22
14	Are things moving around you?	43.5	37	27.5
15	Do you feel dizzy?	13	10	5.5
16	Or unsteady?	28	2	1
17	Is there difficulty in breathing?	28	37	40
18	Do you pass more urine than usual?	19.5	43	44
19	Are you aware of your heart beat?	32.5	21	40
20	Is it faster than usual?	19.5	35	36.5
21	Are you sweating?	37.5	21	25.5
22	Are you hot?	13	12	11.5
23	Or cold?	43.5	37	36.5
24	Are your palms moist?	1	1	3.5

TABLE 6 (continued)

Question number	Question	N = 13		Rank of question		N = 14	
		0	Gamma	25-75	Gamma	100-225	Gamma
25	Are your palms dry?		43.5	46		40	
26	Or cold?		8	43		40	
27	Is your skin sensitive?		24	32		25.5	
28	Do you have funny feelings on your skin?		32.5	9		7	
29	Do your hands and feet feel peculiar?		8	3		5.5	
30	Do they feel heavy?		13	13		9	
31	Or light?		32.5	14		17.5	
32	Is there pressure in your ears?		24	17		15	
33	Is your hearing abnormal?		24	28.5		46	
34	Is it more acute than usual?		24	43		30	
35	Is your eyesight blurred?		32.5	15.5		15	
36	Do you have difficulty in focusing your vision?		43.5	26.5		11.5	
37	Do you see double?		43.5	47		47	
38	Are shapes and colors altered in any way?		37.5	32		31.5	
39	Does light bother you?		32.5	39.5		44	
40	Do things seem too close?		43.5	43		40	
41	Or too far away?		43.5	39.5		33	
42	Do you tremble inside?		16	4		2	
43	Do you feel weak?		32.5	5.5		3.5	
44	Or fatigued?		5.5	5.5		17.5	
45	Do you feel drowsy?		2	8		10	
46	Do you feel as if in a dream?		16	7		8	
47	Are you anxious?		4	15.5		11.5	

It can be seen from Table 6 that some of the questions hold similar relatively important positions in all three groups and that several questions are comparatively insignificant for each group. In some cases questions are ranked similarly for the two drug groups, but differ from the zero dosage group. The exact relationship among rank positions of items within three dosage groups was determined by means of a rank difference correlation coefficient.

TABLE 7
CORRELATION BETWEEN RANK ORDER OF QUESTIONS IN THREE LSD-25 DOSE GROUPS,
COMPARED TWO AT A TIME
(N = 47 questions)

LSD-25 Groups Compared	Correlation coefficient*
0 and 25-75 gamma	.46
0 and 100-225 gamma	.36
25-75 and 100-225 gamma	.83

* Significant correlation coefficient at the .05 level must be .29 and at the .01 level, .37.

Correlation coefficients obtained appear in Table 7. It can be seen that the correlation coefficient between the rank positions of questions in the zero dose group and the 25-75 microgram group was 0.46 and that between the zero group and the high drug group was 0.36. It is important to observe that the ranks of questions in the two drug groups correspond more closely than the ranks of questions in either of the drug groups do with the non-drug groups. In this situation, the correlation coefficient was 0.83. All of these coefficients are statistically significant at the .05 level; all but the 0.36 are significant at the .01 level, and this coefficient practically attains this level of significance.

(3). *Discussion.* The low, but positive, correlations between the zero dose group and each of the drug groups seem to indicate that something other than LSD-25 influenced the response to the questionnaire items. However, the fact that a number of items received little response from subjects in all three groups must not be overlooked. Because of this the ranks of these questions were similarly low and tended to make the correlation positive. The high correlation between item rank of the 25-75 microgram and 100-225 microgram groups shows, however, that the drug does have an effect on physiological and perceptual phenomena which does not appear when a placebo is substituted for the LSD-25. This effect is highly similar in kind at the two doses, but per cent response, intensity of response, and persistency of response may vary. This cannot be determined from a comparison of rank order.

d. Discriminative questions.

(1). *Statistical procedure.* In order to determine which of the 47 questions were responded to significantly more often by members of one dose group than by another, a formula for reliability of the difference between percentages was applied to the data.

Formulae are available for both independent and correlated groups. The groups of subjects previously analyzed were only partially correlated since a number of the subjects were tested at only one level. Since the sample was too small to assume that the uncorrelated portions of these groups are drawn from the same population and are therefore alike, correlated groups only were used in this analysis.

Rather than use groups in which dosages of the LSD-25 vary, a more refined technique was used, and only subjects tested at zero dosage, 50 micrograms of the drug, and 100 micrograms were studied. In this way individual variability, which might be counteracted by the use of different doses of LSD-25, would be avoided and a more accurate measure of the significance of the difference could be obtained.

Results obtained from 11 subjects tested at zero and 50 micrograms were compared; seven who were tested under both zero and 100 micrograms of the drug were compared, and comparison of 10 subjects examined at the two drug levels of 50 and 100 micrograms was made.

The formulae applied to the data were:

$$\rho = \frac{\text{Number of subjects giving plus response in first } 3\frac{1}{2} \text{ hours} \times 100}{N} \quad (4)$$

where ρ equals the percentage of subjects responding positively and N equals the number of subjects in the group;

$$\sigma_{D\%} = \sqrt{\frac{b + c}{N}} \quad (5)$$

where $\sigma_{D\%}$ equals the standard deviation of the difference between percentages, b equals the percentage of subjects responding negatively under the lower dose and positively under the higher, and c equals the per cent of subjects responding negatively under the higher dose and positively under the lower dose:

$$t = \frac{D_{\%}}{\sigma_{D\%}} \quad (6)$$

where $D\%$ equals the difference between the percentages of subjects responding positively under the two doses compared, and t equals the critical ratio. t tables indicate minimum values which must be obtained before rejecting the hypothesis that the true difference between percentages responding under different levels is zero.

Equation 4 was used for deriving percentage positive response rather than Equation 2 since it prevents weighting results to make questions appear more reliable. In this way if a subject reports a symptom at each interval it is considered as only one positive response. Responses in the last two hours of questioning were discarded since not all subjects were quizzed at those times.

(2). *Results.* In Table 8 appear the questions discriminating between zero dosage, and 50 microgram dose groups; that is, these are the questions

TABLE 8
QUESTIONS DISCRIMINATING BETWEEN ZERO AND FIFTY GAMMA LSD-25
(N = 11)

Questions	Percent responding positively in any hour		t
	Zero LSD-25	50 gamma LSD-25	
	<i>.01 level</i>		
	none	none	none
16. Do you feel unsteady?	9	91	3.00
46. Do you feel as if in a dream?	18	91	2.83
	<i>.02 level</i>		
	<i>.05-.03 levels</i>		
28. Do you have funny feelings on your skin?	9	73	2.65
42. Do you tremble inside?	27	91	2.65
32. Is there pressure in your ears?	9	64	2.46
36. Do you have difficulty in focusing your vision?	0	55	2.46
43. Do you feel weak?	18	73	2.46
31. Do your hands and feet feel light?	9	55	2.24
	<i>.10-.06 levels</i>		
12. Are your lips drawn back as if you were smiling?	0	36	2.00
15. Do you feel dizzy?	36	73	2.00
45. Do you feel drowsy?	46	82	2.00
27. Is your skin sensitive?	9	55	1.89
29. Do your hands and feet feel peculiar?	27	73	1.89
	<i>Approx. .10 level</i>		
4. Is salivation increased?	18	46	1.74
6. Is your appetite increased?	27	55	1.74
21. Are you sweating?	18	46	1.74
23. Are you cold?	9	36	1.74
44. Do you feel fatigued?	55	82	1.74

responded to positively by significantly more people under one dose than under the other. At the .01 level, there are no questions that discriminate. At the .02 level, there are two items: (16) "Do you feel unsteady?", where 9 per cent of the zero dose group and 91 per cent of the 50 microgram group responded positively, giving a t of 3.00; and (46) "Do you feel as if in a dream?", where 18 per cent of the zero group and 91 per cent of the 50 microgram group responded giving a t of 2.83. Only two times in one hundred would differences as large as these appear by chance. These were the two most discriminating items between these two dose levels. Between the .03 and .05 levels of significance there were six items which discriminated, and these were: (28) "Do you have funny feelings on your skin?", with a t of 2.65; (42) "Do you tremble inside?", with a t of 2.65; (32) "Is there pressure in your ears?", with a t of 2.46; (36) "Do you have difficulty focusing your vision?", with a t of 2.46; (43) "Do you feel weak?", with a t of 2.46; and (31) "Do your hands and feet feel light?", with a t of 2.24. Items where t values have not reached the .05 level are usually not considered significant statistically. When large samples as great as 1000 are used, a t of 1.96 is necessary for significance at the .05 level; for smaller samples, such as were used in this study, higher values are necessary. However, with the possibility that t values would not vary greatly if this sample were increased questions which have t of about 1.96 are enumerated. These are: (12) "Are your lips drawn back as if smiling?", with a t of 2.00; (15) "Do you feel dizzy?", with a t of 2.00; (45) "Do you feel drowsy?", with a t of 2.00; (27) "Is your skin sensitive?", with a t of 1.89; and (29) "Do your hands and feet feel peculiar?", with a t of 1.89. Percentages responding to the questions appear in the table. There were five items that were significant at almost the .10 level. These were (4) "Is salivation increased?", (6) "Is your appetite increased?", (21) "Are you sweating?", (23) "Are you cold?", (44) "Are you fatigued?". Thus, symptoms which are related to the ingestion of 50 micrograms of lysergic acid diethylamide, and which occur significantly less frequently under a zero dosage, are, in their order of importance: unsteadiness, dreamlike feelings, funny feelings on the skin, inner trembling, pressure in the ears, difficulty in focusing vision, feeling of weakness, feeling of lightness in hands and feet, lips drawn back as if smiling, dizziness, drowsiness, sensitiveness of skin, and peculiar feelings in hands and feet.

Symptoms which appear to have somewhat of a relationship to the drug but are also present, to a lesser extent, among the subjects of the zero group are: increased salivation, increased appetite, sweating, coldness, and fatigue.

The next table under consideration is Table 9, in which the questions discriminating between zero microgram and 100 microgram of LSD-25 appear.

TABLE 9
QUESTIONS DISCRIMINATING BETWEEN ZERO AND ONE HUNDRED GAMMA LSD-25
(N = 7)

Questions	Percent responding positively in any hour		t
	Zero LSD-25	100 gamma LSD-25	
<i>.02-.01 levels</i>			
	none	none	none
<i>.05 level</i>			
14. Are things moving around you?	0	86	2.46
16. Do you feel unsteady?	14	100	2.46
28. Do you have funny feelings on your skin?	0	86	2.46
43. Do you feel weak?	14	100	2.46
46. Do you feel as if in a dream?	14	100	2.46
<i>.10-.06 levels</i>			
1. Do you feel ill in any way?	14	86	2.27
2. Are you nauseated?	0	71	2.27
15. Do you feel dizzy?	29	100	2.27
27. Is your skin sensitive?	0	71	2.27
29. Do your hands and feet feel peculiar?	14	86	2.27
42. Do you tremble inside?	29	100	2.27
21. Are you sweating?	14	71	2.00
31. Do your hands and feet feel light?	0	57	2.00
35. Is your eyesight blurred?	14	71	2.00
36. Do you have difficulty in focusing your vision?	0	57	2.00
41. Do things seem too far away?	0	57	2.00
<i>Approx. .10 level</i>			
3. Have you a feeling of choking?	0	43	1.73
11. Are your lips numb?	0	43	1.73
17. Is there difficulty in breathing?	0	43	1.73
23. Are you cold?	0	43	1.73
32. Is there pressure in your ears?	0	43	1.73
38. Are shapes and colors altered in any way?	0	43	1.73

Seven subjects were studied. There were no questions which discriminated at better than the .02 level. However, at the .05 level, there were five questions that discriminated. These were: (14) "Are things moving around you?", (16) "Do you feel unsteady?", (28) "Do you have funny feelings on your skin?", (43) "Do you feel weak?", and (46) "Do you feel as if in a dream?". All of these items have critical ratios of 2.46. Among the zero group, no more than 14 per cent, or only one subject, ever responded to these questions, while at least 86 per cent and frequently 100 per cent of those in the drug group responded positively to these questions. Between the .06 and the .10 level, eleven items were significant. The six whose *t* values were 2.27 were: (1) "Do you feel ill in any way?", (2) "Are you nauseated?", (15) "Do

you feel dizzy?", (27) "Is your skin sensitive?", (29) "Do your hands and feet feel peculiar?", and (42) "Do you tremble inside?". A minimum of 71 per cent reported these symptoms when under the drug and a maximum of 29 per cent in the zero group gave positive responses. The remaining five items had a critical ratio of 2.00. They were: (21) "Are you sweating?", (31) "Do your hands and feet feel light?", (35) "Is your eyesight blurred?", (36) "Do you have difficulty in focusing your vision?", (41) "Do things seem too far away?". There were six items which were significant at about the .10 level. All of these had a critical ratio of 1.73, and to these six items, none of the people in the zero group ever responded positively, whereas 43 per cent of the people receiving 100 micrograms of LSD-25 responded positively. These were: (3) "Do you have a feeling of choking?", (11) "Are your lips numb?", (17) "Is there difficulty in breathing?", (23) "Are you cold?", (32) "Is there pressure in your ears?", and (38) "Are shapes and colors altered in any way?".

Some of the symptoms highly significant under 50 micrograms are also significant under 100 micrograms. Included in this category are: unsteadiness, dreamlike feelings, feelings of weakness, funny feelings on the skin. Certain symptoms, namely pressure in ears, difficulty in focusing the vision, feeling of lightness in hands and feet, inner trembling, are most significant for the low dose than the high dose, while a new symptom, things moving about, first becomes significant under 100 micrograms.

Among the questions which are significant at the .06-.10 level for the two groups a number of *new* symptoms occur at the high dose: feeling of illness, nausea, sweating, and blurred eyesight.

A comparison of ten subjects tested with 50 and with 100 micrograms (see Table 10) yields very few significant differences in per cent responses to questions despite the comments just made which compare the two groups in a "non-statistical" way. None of the questions discriminate at the .05 level or better. Between the .06 and .10 levels, two items, with critical ratios of 2.00, are significant; (1) "Do you feel ill in any way?", and (30) "Do your hands and feet feel heavy?". At approximately the .10 level, there are four items; (2) "Are you nauseated?", (9) "Do you have a funny taste in your mouth?", (41) "Do things seem too far away?", and (47) "Are you anxious?". For all of these items, although the differences are not highly significant, more people receiving 100 micrograms gave positive responses than those receiving 50 micrograms of LSD-25.

(3). *Discussion.* Unsteadiness and a dream-like state are the main differentiating symptoms between zero and 50 micrograms. These, it would appear, are due to some interference with higher brain processes and possibly

TABLE 10
QUESTIONS DISCRIMINATING BETWEEN FIFTY AND ONE HUNDRED GAMMA LSD-25
(N = 10)

Questions	Percent responding positively in any hour		t
	50 gamma LSD-25	100 gamma LSD-25	
	<i>.05-.01 levels</i>		
	none	none	none
	<i>.10-.06 levels</i>		
1. Do you feel ill in any way?	30	70	2.00
30. Do your hands and feet feel heavy?	30	70	2.00
	<i>Approx. .10 level</i>		
2. Are you nauseated?	40	70	1.76
9. Do you have a funny taste in your mouth?	20	50	1.76
41. Do things seem too far away?	20	50	1.76
47. Are you anxious?	50	80	1.76

involve the ascending reticular pathways, described by Magoun (1) and his workers. Symptoms which discriminate between the .03 and .05 levels (paraesthesias, inner trembling, pressure in the ears, difficulty in focusing, weakness, and lightness of the limbs) are predominantly perceptual changes, and are probably again central in origin and not peripheral. Between zero and 100 micrograms the most discriminating items are those describing things moving around, unsteadiness, paraesthesias, weakness, and dream-like state. They are quite similar in nature to the items differentiating 50 micrograms from zero, with the exception of "things moving around you." Apparently it takes a higher dosage of LSD-25 to elicit vertiginous symptoms. Higher doses of the drug are also required before feelings of illness, nausea, funny taste in mouth, and anxiety are significant. Heaviness of the limbs and objects seeming too far away also occur more frequently under 100 micrograms.

The number of subjects analyzed has considerable influence upon the significance of results obtained. In view of results obtained with small samples, it is likely that more symptoms would be of greater statistical significance if the N were increased. These data, however, indicate the *most reliable* symptoms since they showed differences even with small samples.

While there are not too many items discriminating between 50 and 100 micrograms of LSD-25, and these are not at high levels of significance, it is suggested that the subjective severity of symptoms is greater under the high dose than under the 50 microgram dose. The original response to the questionnaire was made on a one-plus to a five-plus basis and analysis of these responses to questions answered positively by both groups might indicate

differences in severity. The number of subjects used here is too small to warrant this break-down.

Symptoms under 100 micrograms might be experienced more rapidly after ingestion of the drug and might be more persistent than those under 50. The hour-by-hour analysis of responses gave some indication of this. We shall later show that the mean number of symptoms reported each hour tends to support this theory.

Among the items which did not discriminate between dose groups were items to which either a large percentage response or a small percentage response was made by both groups being compared. The former symptoms are probably independent of the pharmacological action of the drug and could be a result of stress and anxiety, environmental conditions, suggestibility of subjects, or some other unknown variable. Only the symptoms which are reported significantly more frequently upon the actual administration of the drug may be ascribed to the action of the drug itself, either directly or indirectly.

2. Number Analysis

a. Number of symptoms reported: Comparison of dosage groups.

(1). *Statistical procedure.* The mean number of symptoms reported during each of the six question periods by subjects in each of the three dosage groups was computed by the following formula:

$$M_{H_i} = \frac{\sum_{i=1}^N + H}{N} \quad (7)$$

where M_{H_i} equals the mean number of symptoms in a given hour, $\sum_{i=1}^N + H$ equals the total number of questions responded to positively in a given hour by all subjects, and N equals the number of subjects. Mean number of symptoms reported per hour during the $5\frac{1}{2}$ hour test period was determined with the formula:

$$M_{PH} = \frac{\sum_{i=1}^6 M_{H_i}}{6} \quad (8)$$

where M_{PH} equals the mean number of symptoms per hour, $\sum_{i=1}^6$ equals the sum of Items 1 through 6, and M_{H_i} equals the mean number of symptoms reported each hour, as calculated with Equation 7.

In order to determine whether differences between the number of symptoms reported by the various dose groups were significantly different from zero and would not have occurred by chance more than five times in a hundred, it was necessary first to compute the mean number of symptoms reported by the same subjects tested at two dose levels. In the comparison between zero and 25-75 micrograms LSD-25, 11 subjects were available for analysis; there were 11 tested at 25-75 micrograms and 100-225 micrograms who were compared, and five whose results under zero and under 100-225 micrograms of the drug were studied. If a subject had been tested at two or more levels within a group, only the data from the lowest dose were used; if a subject had been tested more than once at a given dose, only data from the first testing were used. Equations 9, 10, 11, and 12 were used.

$$M_D = \frac{\sum_{i=1}^N d_i}{N} \quad (9)$$

where M_D equals the mean difference between the number of symptoms reported by groups tested at two levels, d_i equals the difference between the number of symptoms reported by a given subject tested at two levels, and $\sum_{i=1}^N$ equals the sum of 1 to N individuals.

$$SD_D = \sqrt{\frac{\sum x^2}{(N-1)}} \quad (10)$$

where SD_D equals the standard deviation of the difference, $\sum x^2$ equals the sum of the squared deviations of each subject's difference from the mean difference, and N equals the number of subjects.

$$SE_{M_D} = \frac{SD_D}{\sqrt{N}} \quad (11)$$

where SE_{M_D} equals the standard error of the mean difference, SD_D equals the standard deviation of the difference as obtained with Formula 10.

$$t = \frac{M_D}{SE_{M_D}} \quad (12)$$

where t equals the critical ratio, M_D equals the mean difference calculated with formula (9), and SE_{M_D} equals the standard error of the mean difference, calculated with formula (11).

Statistical *t* tables indicate minimum *t* values which must be obtained to warrant rejection of the hypothesis that the real difference between groups is zero.

(2). *Results.* From Table 11 it can be seen that for a group of 11 subjects tested with zero LSD-25 the maximum average number of positive responses occurred $\frac{1}{2}$ hour after the placebo, when 4.9 responses were given. The number of reported symptoms gradually declines thereafter, except for a slight rise at $3\frac{1}{2}$ hours. An average of 3.1 questions per hour received positive responses. It should be noted that one of the 11 subjects was not asked the questions at $4\frac{1}{2}$ and $5\frac{1}{2}$ hours after the drug.

As seen in Table 12, responses made by a group of five subjects given placebos are somewhat similar to those of the groups summarized in the previous table. The maximum response was again given in the first $\frac{1}{2}$ hour

TABLE 11
COMPARISON OF AVERAGE NUMBER OF SYMPTOMS UNDER ZERO LSD-25 AND
25-75 GAMMA LSD-25

(Groups are compared at each of six question periods and for total six periods)

Hours after drug	Average number symptoms Gamma LSD-25		<i>t</i> *	N
	Zero	25-75		
$\frac{1}{2}$	4.9	4.3	.44	11
$1\frac{1}{2}$	4.1	13.2	4.11	11
$2\frac{1}{2}$	2.3	13.5	7.03	11
$3\frac{1}{2}$	2.9	12.0	4.46	11
$4\frac{1}{2}$	1.8	9.5	4.05	10
$5\frac{1}{2}$	1.8	10.0	3.34	10
Average $5\frac{1}{2}$	3.1	10.6	5.71	11

* See Table 14 for values of "*t*" at the different levels of significance.

TABLE 12
COMPARISON OF AVERAGE NUMBER OF SYMPTOMS UNDER ZERO LSD-25 AND 100-225
GAMMA LSD-25

(Groups are compared at each of six question periods and for total six periods)
N = 5

Hours after drug	Avg. No. Symptoms Gamma LSD-25		<i>t</i> *
	Zero	100-225	
$\frac{1}{2}$	3.8	9.4	1.99
$1\frac{1}{2}$	1.8	19.0	6.25
$2\frac{1}{2}$	3.0	18.2	4.75
$3\frac{1}{2}$	2.6	16.2	3.22
$4\frac{1}{2}$	1.8	14.2	2.29
$5\frac{1}{2}$	1.8	12.4	4.17
Average $5\frac{1}{2}$	2.5	14.9	6.10

* See Table 14 for values of "*t*" at the different levels of significance.

when an average of 3.8 questions were answered positively. After the decrease at 1½ hours there was an increase, after which the number of symptoms declined. The average number of symptoms throughout the day was 2.5, which is .6 symptoms less than for the group of 11 subjects.

The average number of symptoms reported per hour by the 25-75 microgram group was 10.6 for an "N" of 11 (see Table 11) and 8.9 (see Table 13) for another group of 11 subjects some of whom were the same. The peak hour was at 2½ hours for one group and 1½ hours for the other. In each group, however, the difference between symptoms reported at 1½ and 2½ hours is negligible and the time of greatest reaction to the drug may be thought of as extending from 1½ to 2½ hours after the drug. A decrease in positive responses followed for both groups, with a slight increase at 5½ hours.

TABLE 13
COMPARISON OF AVERAGE NUMBER OF SYMPTOMS UNDER 25-75 GAMMA LSD-25 AND
100-225 GAMMA LSD-25
(Groups are compared at each of six question periods and for total six periods)

Hours after drug	Avg. No. Symptoms		t*	N
	25-75 Gamma	100-225 Gamma		
½	5.4	12.0	3.13	11
1½	11.9	16.7	3.77	11
2½	11.8	15.1	1.64	11
3½	9.8	14.6	2.16	10
4½	6.9	13.3	2.95	10
5½	10.8	13.8	1.07	4
Average 5½	8.9	13.6	4.48	11

* See Table 14 for values of "t" at the different levels of significance.

Under 100-225 micrograms five subjects gave an average 14.9 positive responses per hour, while a group of 11 reported an average of 13.6 symptoms each hour. In both groups the peak hour occurred 1½ hours after the drug; following this peak there was a very slight decline. By the last question hour as many as 12.4 and 13.8 positive responses were still being made. This indicates that the drug effects may persist for a more extended period with high dosage.

Despite the variability between each pair of the three dose groups, the number of positive responses is correlated with the amount of drug; increasing amounts of drug and greater number of reported symptoms, out of the 47 suggested ones, tended to occur together. A statistical analysis of the differences between the number of positive responses made each hour by each group indicate whether the differences would have occurred by chance or whether they are true differences. The *t* values, or critical ratios, reported in Tables 11-13 may be interpreted with the aid of Table 14. The minimum

values of t which must be obtained before a difference for a given sample size can be considered significant are given in this table.

TABLE 14
"t" VALUES AT FOUR LEVELS OF SIGNIFICANCE
(Values are given for various "N's" used in comparisons made in Tables 11, 12, and 13)

N	Degrees of freedom	.10	levels of significance			.01
			.05	.02		
			"t" values			
4	3	2.35	3.18	4.54	5.84	
5	4	2.13	2.78	3.75	4.60	
7	6	1.94	2.45	3.14	3.71	
10	9	1.83	2.26	2.82	3.25	
11	10	1.81	2.23	2.76	3.17	
∞	∞	1.65	1.96	2.33	2.58	

In comparing 0 with 25-75 micrograms the differences between symptoms reported at each period but the first are significant and would have occurred by chance less than one time in a hundred (see Table 11). While a minimum t of 3.17 was necessary for .01 level significance, all values were above this. The most reliable difference appeared at $2\frac{1}{2}$ hours, the peak hour for the 25-75 group.

When the high drug group is compared to the zero dose group, the differences at the $\frac{1}{2}$ and $4\frac{1}{2}$ hour intervals were not significant (at the .05 level). However, all the other hours showed differences significant at the .05 level or better. Here too, the most significant differences were seen at the peak hour of the drug group which was $1\frac{1}{2}$ hours. These results are seen in Table 12.

Less striking and less reliable differences are observed in analyzing the 25-75 and 100-225 microgram groups. Although the average number of symptoms per hour show a difference reliable at better than the .01 level, the only significant hours (as shown in Table 14) are the first $\frac{1}{2}$ hour (significant at the .05 level), $1\frac{1}{2}$ hours (significant at better than the .01 level) and $4\frac{1}{2}$ hours (significant at better than the .02 level, but not at the .01 level). The required "t" values are given in Table 14.

The foregoing results indicate that LSD-25 does have an effect upon the physiological and perceptual status of the individual, with greater amounts of drug producing greater effect, as determined by the number of positive responses to the 47 items on the questionnaire. About three symptoms on the average, are reported under a placebo, about 10 under 25-75 micrograms of the drug, and about 14 under 100-225 micrograms (Tables 11, 12, and 13).

(3). *Discussion.* Although the standard deviation of scores about the

mean is not reported in the tables, there is a certain scatter about the mean; consequently when a different group of subjects is tested it is not likely that the identical means will be obtained for each group examined under comparable conditions. This was observed in results obtained. However, despite the differences between means for the same dose group, the differences are small when compared to the differences between dose groups.

The statistics indicate that the high dose of drug takes effect as early as $\frac{1}{2}$ hour after ingestion, while the low dose gives responses similar to the zero dose group at that hour. In addition to its more rigid effectiveness the high dose produces more persistent symptoms. The average number of symptoms reported by the 100-225 group at each hour is greater than the maximum number of the low dose group, as shown in Table 13. At $2\frac{1}{2}$ hours, the difference between these two groups is not significant. In the low group, the peak seems to occur between $1\frac{1}{2}$ and $2\frac{1}{2}$ hours, with little difference between number of symptoms at these two periods. The high group peak is definitely at $1\frac{1}{2}$ hours, and declines thereafter. Thus the difference at $2\frac{1}{2}$ hours becomes insignificant. The last hour ($5\frac{1}{2}$) also shows no reliable difference. However, there were only four subjects questioned at this hour, and thus the means are less reliable than for the other hours, and this comparison deserves less consideration.

The increase in number of symptoms reported by the 25-75 microgram group in the last hour, as shown in the group compared with the zero dose group (Table 11) appears to be too small to be significant. A larger increase is observed at this hour when the 25-75 and 100-225 microgram groups are compared. However, only four subjects were tested at this level, in contrast to 10 or 11 subjects examined during the previous hours. The results for the last hour are not comparable to the rest of the results and the rise in mean number of symptoms may be disregarded.

Despite the observation earlier in this report that only a relatively small number of the 47 items on the questionnaire were significant items, it is interesting that comparison among groups, of number of symptoms reported shows definite differences. With increasing dosage there is also an increased tendency to respond positively. It is suggested that if the responses made to only the significant questions were analyzed in the same way, far greater differences having far greater significance would be found.

b. Relationship between subjects responding at different doses.

(1). *Statistical procedure.* To investigate the significance of the individual subject the rank difference correlation coefficient is computed with Formula (3) given previously:

$$\rho = 1 - \frac{6\sum D^2}{N(N^2 - 1)} \quad (3)$$

where ρ equals the rank difference correlation coefficient, D equals the difference between the rank of an individual in one dose group and his rank in another group; rank 1 is delegated the subject reporting the fewest mean number of symptoms per hour, etc.; and where $\sum D^2$ equals the sum of the squared differences in rank for all subjects in the groups compared, and N equals the number of subjects.

Once again the three dose groups were compared two at a time, with only correlated groups used. The number of subjects in each pair of groups was as follows: (a) zero and 25-75 micrograms LSD-25 (11); (b) zero and 100-225 micrograms LSD-25 (5); (c) 25-75 micrograms and 100-225 micrograms LSD-25 (11).

If subjects were tested at two levels in a given dose group, data from only the lowest level were used; if a subject was tested more than once at a given level, data from only the first testing were used.

(2). *Results.* The rank difference correlation coefficients of the average number of symptoms reported per hour by subjects tested at three different dose levels, compared two at a time are given in Table 15. Between the zero

TABLE 15
CORRELATION BETWEEN AVERAGE NUMBER OF SYMPTOMS REPORTED PER HOUR BY
SUBJECTS AT 3 LSD-25 DOSE LEVELS

LSD-25 Dose Groups compared	N	Correlation coefficient	Significant Corr. Coef.	
			.05 level	.01 level
zero and 25-75 gamma	11	.66	.60	.74
zero and 100-225 gamma	5	.60	.88	.96
25-75 and 100-225 gamma	11	.90	.60	.74

and 25-75 microgram groups there were 11 subjects and the correlation between their ranks in the two groups (according to the number of symptoms they reported) was .66. This is significant at somewhere between the .01 and .05 level. Between zero and 100-225 micrograms, where there were only five subjects, the correlation was .60. For this number of subjects, the correlation is not significant at the .05 level. With a greater number of subjects, significance would probably be reached. Between the 25-75 and 100-225 microgram level, there was a correlation of .90 for 11 subjects; this is significant at better than the .01 level.

(3). *Discussion.* The results obtained in this analysis are highly important in indicating the significance of the individual subject. The extremely

high, almost perfect, correlation between results of the two groups that took LSD-25 indicates that the person reporting relatively little effect under an intermediate dose will also report relatively little effect under a high dose. Similarly, the person in the group who responds positively to more questions than other subjects tested at a low dose will respond similarly at a high dose.

Previously discussed data showed that a reliably greater number of symptoms (see Table 13) was reported under the high dose than under the low dose. The results reported in Table 15 show that despite the fact that subjects gave more positive responses under 100-225 micrograms, the response made seems to be a function of another factor in addition to LSD-25.

The high correlation between an individual's rank position at zero dose and each of the two drug groups has even more interesting implications. While the correlations are not perfect, they are sufficiently high to permit a fair amount of accuracy in predicting whether an individual will show a small or large reaction under the drug, on the basis of his reaction under zero dosage. There are apparently unknown factors in a given individual which make him more or less suggestible at each level of dosage.

c. Consistency of response under same dose.

(1). *Statistical procedure.* The Pearson product-moment correlation coefficient was calculated to show the relationship between results obtained under two testings of a given subject under the same dose. The number of symptoms reported at each of the six question intervals and the average number of symptoms per hour under the two testings were compared by Equation (13).

$$r = \frac{N\Sigma XY - \Sigma X \times \Sigma Y}{\sqrt{[N\Sigma X^2 - (\Sigma X)^2] [N\Sigma Y^2 - (\Sigma Y)^2]}} \quad (13)$$

where r equals the coefficient of correlation, N equals the number of subjects, X equals the number of symptoms reported during the first testing, and Y equals the number of symptoms reported during the second testing. Nine subjects were studied in this manner. While each subject was tested twice at a given dose, the doses ranged from 25 micrograms to 200 micrograms of the drug. One subject was tested twice at each of three dosages; his responses at the first testing under each dose were average, and those of the second testings were averaged.

(2). *Results.* The data tabulated in Table 16 gives some measure of the reliability of responses made to the questionnaire under the influence of lysergic acid diethylamide. The closer the correlation coefficient is to 1.00,

TABLE 16
CORRELATION BETWEEN NUMBER OF SYMPTOMS REPORTED AT TWO SEPARATE TESTINGS
UNDER SAME LSD-25 DOSAGE
(N = 9)

Hours after LSD	Correlation coefficient*
$\frac{1}{2}$	.34
$1\frac{1}{2}$	.42
$2\frac{1}{2}$	.45
$3\frac{1}{2}$	.63
$4\frac{1}{2}$	.58
$5\frac{1}{2}$	.72
Total $5\frac{1}{2}$	.77

* Correlation coefficients must equal .67 to be significant at the .05 level, and .80 to be significant at the .01 level.

the more likely it is that second testings under the same dose will elicit the same number of responses. The following coefficients were obtained:

At the first $\frac{1}{2}$ hour, there was a correlation coefficient of 0.34; at the $1\frac{1}{2}$ hour interval it was 0.42; at $2\frac{1}{2}$ hours, it was 0.45; at $3\frac{1}{2}$ hours, it was 0.63; at $4\frac{1}{2}$ hours, it was 0.58; and at $5\frac{1}{2}$ hours, 0.72. Thus, the correlation coefficient tends to increase with increasing time after administration of LSD-25. Only the coefficient at $5\frac{1}{2}$ hours after the drug is significant at the 0.5 level.

The correlation coefficient between the total number of symptoms reported under the two testings was .77. This is significant at the .05 level and almost reaches significance at the .01 level. Thus, on the whole, it can be said that the number of responses to a specified dose is fairly constant for each individual.

(3). *Discussion.* It seems unusual that a correlation coefficient as high as .72 would be obtained for the last testing hour, when the previous hours showed lower correlations. However, this is probably a function of the smaller number of symptoms reported in the last hour.

The correlations obtained at each of the other hourly intervals might be more reliable and higher if a greater number of subjects were used. The fact that the correlation for the total number of symptoms during the day is significant (and higher) tends to support this hypothesis, since this figure was based on a larger number of observations.

The fact that only some of the questions in the questionnaire are significant questions in terms of LSD-25 effects, might contribute to the lack of reliable and high correlation coefficients. Recalculation of these coefficients in terms of the number of discriminating questions reported at the two testings might produce results indicating greater consistency in reporting "reliable" symptoms.

d. Relationship between body weight and symptoms reported.

(1). *Statistical procedure.* The subject's reported body weight and the number of questions to which he responded positively at each of three LSD-25 doses (0 micrograms, 50 micrograms, and 100 micrograms) were compared by Equation 13a for periods of $\frac{1}{2}$ hour and $1\frac{1}{2}$ hours after the drug to determine the relationship between the two.

$$r = \frac{N\sum XY - \sum X \times \sum Y}{\sqrt{[N\sum X^2 - (\sum X)^2][N\sum Y^2 - (\sum Y)^2]}} \quad (13a)$$

where r equals the coefficient of correlation, N equals the number of subjects, X equals the figure representing the subject's body weight, and Y equals the number of symptoms reported by subject of body weight X . The standard deviation of r was then computed by the formula:

$$\sigma_r = \frac{1 - r^2}{\sqrt{N - 1}} \quad (14)$$

where σ_r equals the standard deviation of correlation coefficient, r^2 equals the squared correlation coefficient, and N equals the number of subjects.

Appropriate statistical tables indicate minimum coefficients which must be obtained under different sample sizes before the coefficients are considered reliably different from zero.

(2). *Results.* In Table 17, the correlations between the number of symptoms reported at a given dosage and the subject's body weight in pounds are given. At zero dosage, for the first $\frac{1}{2}$ hour, the correlation is 0.20, with a standard deviation of 0.28; this correlation is not significantly different from zero, for an N of 13, as indicated in the table. At this same dosage, but $1\frac{1}{2}$

TABLE 17
CORRELATION BETWEEN NUMBER OF SYMPTOMS REPORTED AND SUBJECT'S BODY WEIGHT
(Zero, 50, and 100 gamma are analyzed for $\frac{1}{2}$ and $1\frac{1}{2}$ hours after LSD-25)

Amt. LSD-25	Hours after LSD-25	r	σ_r	N	Significant correlation coefficients	
					.05 level	.01 level
zero	$\frac{1}{2}$	.20	.28	13	.55	.68
zero	$1\frac{1}{2}$	.49	.22	13	.55	.68
50 gamma	$\frac{1}{2}$	.02	.26	16	.50	.62
50 gamma	$1\frac{1}{2}$	.18	.25	16	.50	.62
100 gamma	$\frac{1}{2}$	.39	.26	12	.58	.71
100 gamma	$1\frac{1}{2}$	.17	.29	12	.58	.71
				1000	.06	.08

hours after the placebo, the correlation is 0.49, the standard deviation 0.22; this almost reaches significance at the .05 level. At 50 micrograms, the correlation between body weight and the number of symptoms reported at the first $\frac{1}{2}$ hour is 0.02, ($\pm .26$) which is not significantly different from zero. At $1\frac{1}{2}$ hours, the correlation is 0.18 with a standard deviation of 0.25, so this is not significant. Under 100 micrograms of LSD-25 the correlation is 0.39, ($\pm .26$) for the first $\frac{1}{2}$ hour; $1\frac{1}{2}$ hours after the drug the correlation is 0.17, ($\pm .93$). None of these correlations is significant even at the .05 level. If a larger number of subjects were used it is possible that some of these correlations, if they remained the same, would become significant. For an N of 1000, it would only be necessary to have a correlation of .08 to reach the .01 level, or a correlation of .06 to reach the .05 level of significance. All the obtained correlations, but one, are higher than these values. None of the correlations were significantly different from zero for the number of subjects evaluated. It can be said that there is no relationship between the subject's body weight and the number of symptoms he reports on the questionnaire.

(3). *Discussion.* The literature on experiments investigating lysergic acid diethylamide symptomatology frequently reports use of dosages in proportion to body weight; generally one microgram of drug per kilogram of body weight has been given "normals." This practice is based on the theory of pharmacologic drug action that a larger and heavier person would have a smaller concentration of the drug than a smaller person receiving the same amount of drug if the substance were evenly dispersed through the body.

The correlation coefficients obtained fail to justify this procedure. Although increased sample size might yield different results, coefficients would have to be negative to support the theory of relatively less drug effect upon heavier persons. It is highly unlikely that results from larger samples would become greater in absolute value, and be opposite in direction. The obtained correlation coefficients are all positive and thus, if a larger N made them significant, they would indicate that heavier subjects report a greater rather than a smaller number of symptoms.

It is of interest to note that the highest and most significant correlation was obtained when only a placebo was given the subjects, suggesting that heavier persons are more suggestible. Whether weight is directly responsible or not cannot be determined.

D. SUMMARY AND CONCLUSIONS

On the basis of tests performed on 26 non-psychotic, intelligent adults, who were given from one to three doses of lysergic acid diethylamide (zero, 25-75 micrograms, and 100-225 micrograms), and to whom a questionnaire, in-

vestigating changes in physiological and perceptual phenomena, was given at hourly intervals, the following conclusions are drawn:

1. Symptoms most significantly related to the ingestion of 50 micrograms of the drug are (in order of decreasing significance): unsteadiness, dream-like feeling, paraesthesias, inner trembling, pressure in ears, difficulty in focusing vision, weakness, lightness of limbs, lips drawn back as if smiling, dizziness, drowsiness, sensitivity of skin, and peculiar feeling of limbs. Less significant, but probably related, are: increased salivation, increased appetite, sweating, cold, and fatigue.

2. Symptoms most significantly related to the ingestion of 100 micrograms of the drug are (in order of decreasing significance): things moving about subjects, unsteadiness, paraesthesias, weakness, dream-like feeling, illness, nausea, dizziness, sensitivity of skin, peculiar feeling of limbs, inner trembling, sweating, lightness of limbs, blurred eyesight, difficulty in focusing vision, and objects seeming too far away. The less significant but probably related symptoms are: feeling of choking, numbness of lips, difficulty in breathing, cold, pressure in ears, and alteration of shapes and colors.

3. There may be differences in subjective severity and quality of the symptoms which are reported under both drug levels. However, several symptoms discriminate between 50 and 100 micrograms in that they received a greater percentage of response under the high dose. These are: feeling of illness, heaviness of limbs, nausea, funny taste in mouth, objects seeming too far away, and anxiety.

4. There is a significant correlation of .83 between the relative position of symptoms, according to frequency of positive response, for the two drug groups.

5. The average number of symptoms, out of 47 suggested ones, under zero dosage is about 3; under 25-75 micrograms it is approximately 10; and under 100-225 micrograms it is about 14. The differences among the three groups are all statistically reliable at better than the .01 level of significance.

6. The peak effect under zero dosage occurs in the first $\frac{1}{2}$ hour, and that of the low dose between $1\frac{1}{2}$ and $2\frac{1}{2}$ hours after the drug. The peak for the high dose occurs $1\frac{1}{2}$ hours after the drug, and the effect is longer lasting than for either of the other groups. These statements are based on group results and individual variability is not considered here.

7. The number of symptoms a subject reports under the low dose correlates .90 with the number he reports under the high dose. Although the average number of symptoms increases, he maintains his relative position within the group. There is also a relationship as high as .66 and .60 between subjects relative position under zero and under low and high doses of LSD-25, respectively. This indicates a fairly high degree of predictability of the number of

responses to the drug on the basis of the number of responses under the placebo.

8. The reliability of responses to the questionnaire has been found high. Test-retest correlation as high as .77 was obtained in comparing the total number of symptoms reported at two separate testings under the same dosage.

9. The number of symptoms reported and the subject's body weight have been shown either to be unrelated or not related in the expected direction.

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