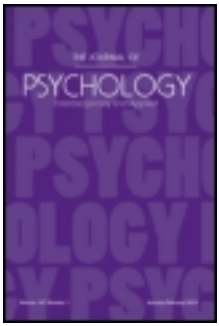

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LYSERGIC ACID DIETHYLAMIDE (LSD-25): XV. THE EFFECTS PRODUCED BY SUBSTITUTION OF A TAP WATER PLACEBO*

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A. INTRODUCTION

The purpose of this paper is to study the responses given to a questionnaire by subjects who received a tap water "placebo" instead of lysergic acid diethylamide (LSD-25), and to relate the number of responses to other variables. These variables are: body weight, number of responses on a health questionnaire, arithmetic test scores, scores on the Wechsler-Bellevue Intelligence Scale, and Rorschach test responses.

Although the word "placebo" translated means "I shall please," the word in medicine generally involves the concept that a relatively inert substance is given to a patient for either psychotherapeutic purposes or for experiments designed to test the activity of another drug. An interesting review of the whole problem connected with the administration of placebos to patients appears in Lilly's "Physicians' Bulletin" (10, 11) for January and February, 1955.

The data presented in this communication encompass a set of circumstances somewhat different from those in which a placebo is ordinarily used. In the experiments to be reported here, the subjects expected to get a dose of lysergic acid diethylamide which would produce either a relatively mild or a relatively severe response, the severe response being in the nature of a temporary psychosis. For this reason when the dose of LSD-25 was zero, the "placebo" in this case was not a drug which was "striving to please" but which psychodynamically was attempting to induce a structured psychosis because of the way in which the results of the experiments were limited, to a certain extent, by the questionnaire employed and the attitudes of the

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[2]We are indebted to Sandoz Pharmaceuticals, Inc., for supplies of LSD-25 and other compounds.

investigators. The details of the technique of administration of both drug and questionnaire are enumerated in an earlier paper of this series (1) and will be discussed under Method.

The use of placebos in a population with neuropsychiatric symptoms is very well illustrated by the paper of Hampson, Rosenthal, and Frank (4) where a placebo was studied to ascertain the specific effect of mephenesin on the symptomatology of a mixed group of psychiatric outpatients presenting a wide range of psychiatric symptoms. They found a decline in severity of symptoms with *both* mephenesin and the placebo. In our data there is no attempt to look for a sign of therapeutic efficacy but only for the symptomatology of the structured psychological responses enumerated in the questionnaire. Our zero dose of LSD-25 or placebo dose should be classified as a negative placebo *because only symptomatic exacerbation may occur.* It is of interest to quote the data of W. B. Tucker (13) who, in a somewhat analogous situation with streptomycin, found that 60 per cent of patients receiving placebo injections instead of streptomycin showed one or more manifestations of streptomycin toxicity, including hearing loss, eosinophilia, and impairment of urea clearance. Similarly, Wolf and Pinsky (13), using physically inert placebos in patients having anxiety and tension as prominent complaints, reported that lightheadedness, drowsiness, weakness, palpitation, and nausea as well as skin eruptions could occur in addition to diarrhea, urticaria, and angioneurotic edema.

B. Method

1. *Subjects*

There were 33 paid, adult volunteers, 16 males and 17 females. Ages ranged from 22 to 39 years with the median at 26. The median weight was about 150 pounds, ranging from 103 to 203. All but two subjects were considered non-psychotic according to a psychiatric interview and certain clinical psychological tests described in a previous paper (1). One subject was judged psychotic on the basis of these tests and one subject was not pre-tested. These subjects were included in the sample since their responses to the questionnaire used here fell within the range of the responses of the non-psychotic group. The intelligence of the group was average or above, as determined by the Wechsler-Bellevue Intelligence Scale. There were 19 graduate students, a college student, a law student, 3 housewives, and 9 employed subjects whose occupations varied widely.

2. *Tests*

The questionnaire used to assess the responses to 75 cc of tap water (given in lieu of lysergic acid diethylamide) inquired about the subject's physiological and perceptual state. There was a total of 47 questions which appear in Figure 4 of the present paper. The questionnaire is reproduced in a previous paper. Five of the 33 subjects responded to a revised questionnaire (5) based on statistical analysis of the responses to the first questionnaire. In the revision the items from the original questionnaire which did not differentiate between the placebo and the drug groups did not appear and the ambiguous items were clarified. A series of questions on the cognitive state of the subject was added.

The number of responses to the questionnaire was compared with subject's body weight, and with his responses to the following: Cornell Medical Index Health Questionnaire (2), Arithmetic test (6), Rorschach test (9), and the Wechsler-Bellevue Intelligence Scale (8).

3. *Procedure*

a. Drug and test administration. With two exceptions, the first experiment in which a subject participated was the control or placebo experiment where he received only 75 cc of tap water, orally, and no LSD-25. One subject had taken LSD-25 once before the placebo experiment and another had received it four times before receiving a placebo. Since LSD-25 is tasteless, odorless, and colorless, and is given in 75 cc of tap water, the subjects could not detect that they received only water. Subjects were tested in groups of two to five. Some subjects in these groups received a placebo; some received the drug and exhibited "typical" LSD-25 symptoms as described in a previous paper (1).

The placebo was administered between 9:30 and 11:40 A.M. Those receiving it at 9:30 ate no food before. About ½ hour later they ate a light breakfast and about 2½ hours later they ate lunch. Those receiving it after 9:30 A.M. had eaten breakfast between 7:00 and 8:00 A.M., and ate lunch about noon. Fifteen subjects responded to the questionnaire ½ hour after receiving the placebo and at hourly intervals thereafter, up to 4½ hours. Eighteen responded ½, 2½, and 4½ hours after ingestion of the placebo; five subjects also responded before receiving the placebo. A response of zero indicated that the symptom was not present. If the subject wished to indicate that the symptom was present he responded on a + to + + + + + scale, according to his subjective evaluation of the severity of the symptom. A

+ response signified only slight intensity of the symptom. A + + + + + response indicated relatively great intensity of the symptom. The ratings among subjects are not comparable since the definition of each point on the rating scale was a subjective one made by each subject for himself. On the revised questionnaire, the maximum positive response was limited to + + +.

Responses to the Rorschach ink blots and the Wechsler-Bellevue Intelligence Scale were obtained during the pre-testing session under non-drug conditions. The Cornell Medical Index Health Questionnaire was completed by subjects either during the pre-testing session or after the series of placebo and drug experiments had been completed. The arithmetic test was given during the experimental day and was one of many tests given at that time.

b. Method of analysis. Two major types of analysis were made: (*a*) the nature of the responses to the questionnaire and, (*b*) the relationship between the number of positive responses to the questionnaire and performance on other tests.

The analysis of the questionnaire included the tabulation of the total number of positive responses made by each subject during each interval and the total number of different questions responded to positively during three time intervals. The average number of responses at each interval, the peak hour, and the percentage of subjects responding to each question were also determined.

The Pearson product-moment correlation coefficient (3) related the number of different symptoms reported during three intervals (½, 2½, and 4½ hours after the placebo) with the number of "yes" responses given on the Cornell Medical Index Health Questionnaire, the number of correct solutions on the arithmetic test, and the body weight of the subjects. The six non-psychotic subjects giving the least number of different responses during three time intervals were compared with the six non-psychotic subjects giving the greatest number of different responses during these time intervals. The scores of the two groups on each of the subtests of the Wechsler-Bellevue test, their Performance Scale *IQ*, their Verbal Scale *IQ*, and their Full Scale *IQ* were compared by means of the Wilcoxon non-parametric technique of unpaired replicates (12) to determine whether there were significant differences between the "low" response and "high" response groups. The scores of the two groups on the quantitative variables of the Rorschach test were also compared by this method.

A third group of six subjects whose number of reported symptoms placed them in a "middle" symptom group was compared with the "low" and

"high" group to determine whether their scores on the Wechsler-Bellevue Intelligence Scale and Rorschach test fell between those of the other two groups. Differences among groups in scores on these two tests might enable us to understand some of the personality and intellectual factors which are related to suggestibility, as measured by the number of responses to the questionnaire.

The correlations computed and statistical comparisons made are based only on the 28 subjects who completed the original questionnaire, and do not include the five subjects tested with the revised questionnaire. There were too few subjects in the latter group for statistical analysis, and the range of responses was too narrow to permit grouping of the subjects into "high" and "low" response groups.

C. Results

Figure 1 shows each subject's course of reaction to the placebo dose. A separate subgraph for each of the 33 subjects shows the total number of positive responses each made to the questionnaire at stated time intervals after the ingestion of the placebo. The ordinate of each subgraph is the total number of positive responses made. The abscissa is the time in hours after receiving the placebo. The subgraphs of Subjects 1 through 28 are arranged in order of increasing response according to the total number of different questions responded to positively during the ½-, 2½-, and 4½-hour periods. Where several subjects gave the same number of different responses, they are arranged in order of increasing total number of responses during the same three intervals. Subjects 29 through 33 responded to the revised questionnaire and therefore appear as a separate group.

Subjects 1 and 2 gave no positive responses throughout the day, while Subject 28 gave as many as 15 different responses during three time intervals, and Subject 22 different responses during four time intervals. Eleven subjects gave the greatest number of responses ½ hour after the ingestion of the placebo; six showed the greatest effect at 2½ hours. Two subjects had the peak effect 1½ hours after, one had it 3½ hours after, and one 4½ hours after receiving the placebo. The remaining seven subjects tested with the original questionnaire did not have a single peak hour. Subjects 29 through 33 who responded to the revised questionnaire never gave more than four positive responses in any one hour. They differed with regard to the peak hour.

The number of different positive responses made during three intervals by the group of 28 subjects ranged from zero to 15. Figure 2 shows the

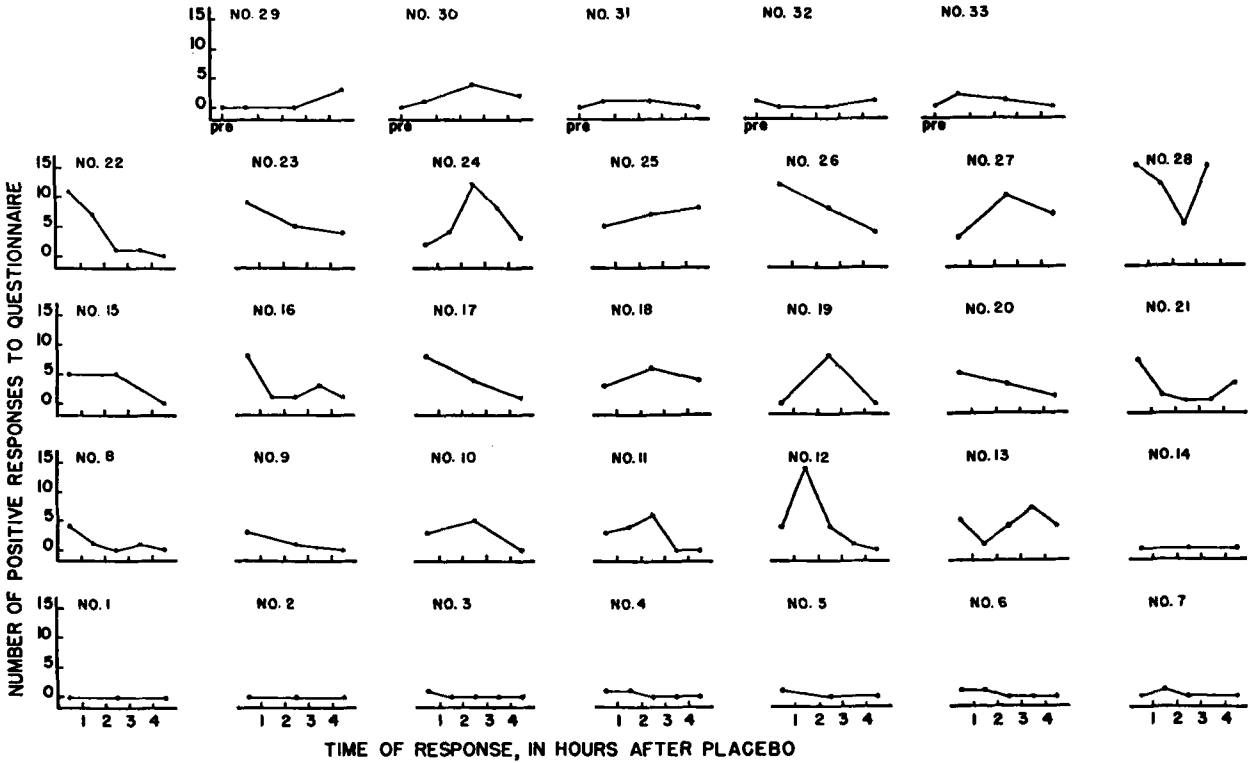

FIGURE 1

NUMBER OF POSITIVE RESPONSES TO QUESTIONNAIRE AT STATED TIME INTERVALS AFTER THE INGESTION OF A PLACEBO
Subjects 1 through 28 are arranged in order of increasing number of different responses. Subjects 29 through 33 responded to the revised questionnaire.

number of different positive responses made and the percentage of subjects who made them. By adding the percentages of adjacent bars it appears that 25 per cent of the group gave up to three positive responses and 25 per cent gave between 4 and 6. The third quarter of the group gave

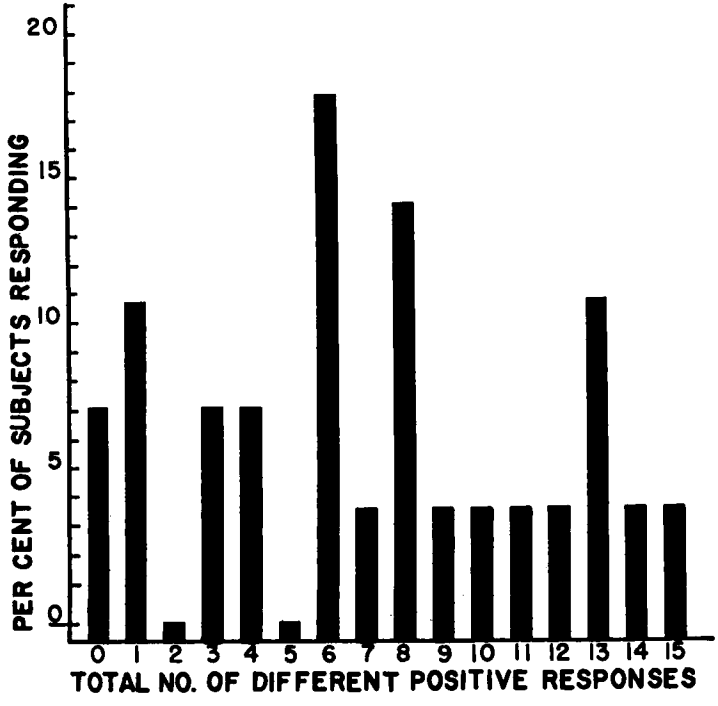

FIGURE 2
DISTRIBUTION OF TOTAL NUMBER OF DIFFERENT POSITIVE RESPONSES AND PERCENTAGE OF SUBJECTS GIVING EACH

between 7 and 10 different positive responses and the upper quarter gave between 11 and 15.

The average number of positive responses given at stated time intervals by a group of 15 and of 13 subjects appears in Figure 3. The group of 15 responded five times during the day while the group of 13 responded only three times. The greatest number of responses was made ½ hour after the ingestion of the placebo by the group of 15, and the least number was made 4½ hours after. The average number of responses by the group of 13 show that the maximum occurred 2½ hours after the placebo, and

the minimum 4½ hours later. When subjects received LSD-25 the greatest number of positive responses, on the average, was given at 1½ or 2½ hours, depending on the dose. The lowest response occurred at 4½ hours (1).

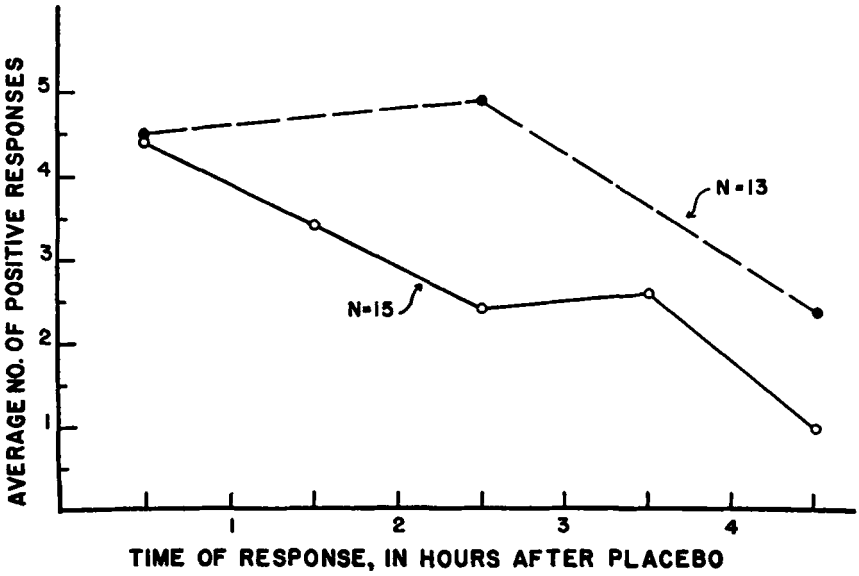

FIGURE 3
AVERAGE NUMBER OF POSITIVE RESPONSES GIVEN BY EACH OF TWO GROUPS OF SUBJECTS AT STATED TIME INTERVALS AFTER THE INGESTION OF A PLACEBO
(The original questionnaire was used)

Figure 4 shows for each question the percentage and number of subjects out of 28 who gave a positive response at least once during the ½-, 2½-, and 4½-hour intervals. The questions appear in the figure in the order of decreasing percentages of response to them. The time of the response and the magnitude are disregarded in this tabulation. The question receiving the greatest percentage response was (Subject 24), "Are your palms moist?" As many as 60.7 per cent reported this symptom. Half of the subjects reported headache (Subject 13), fatigue (Subject 44), and drowsiness (Subject 45). About 36 per cent reported anxiety (Subject 47). Illness (Subject 1), and dizziness (Subject 15) were reported by 28.6 per cent of the group and 25 per cent indicated a dream-like feeling (Subject 46), increased appetite (Subject 6), unsteadiness (Subject 16), a hot feeling (Subject 22), heaviness of hands and feet (Subject 30), and weakness (Subject 43). There were 19 questions which received positive responses from

between 10 and 22 per cent of the subjects. Less than 10 per cent of the group (or no more than two subjects) responded positively to the remaining questions, but each question received a positive response from at least one subject.

The relationship between the number of positive responses made by a subject and his response on other tests is summarized in Table 1 where the

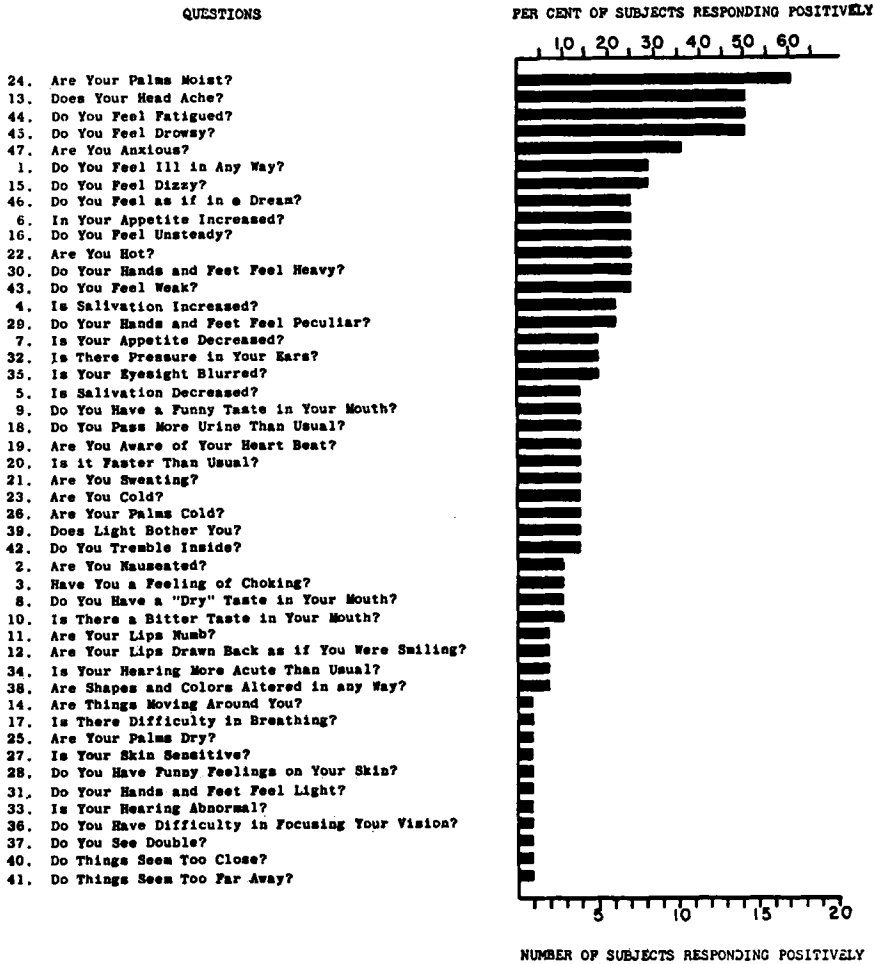

FIGURE 4

THE NUMBER AND PERCENTAGE OF 28 SUBJECTS RESPONDING POSITIVELY TO THE ITEMS OF THE QUESTIONNAIRE

(Questions are arranged in order of decreasing percentage response)

Pearson product-moment correlation coefficients are given. The coefficient relating the number of positive questionnaire responses with the number of "yes" responses made on the Cornell Medical Index Health Questionnaire

TABLE 1

PEARSON PRODUCT-MOMENT CORRELATION COEFFICIENTS
(Number of questionnaire responses is correlated with other measures)

Item correlated with number of positive responses on questionnaire	*r*	*N*
1. Number of "yes" responses on Health Questionnaire	—.05	20
2. Arithmetic test scores	.52	11
3. Body weight of subject	.28	27

Note: With the given *N*, for each correlation the probability of chance occurrence is $>.05$.

is —.05. A correlation of .52 was obtained for the relationship between the questionnaire responses and the arithmetic test scores. The body weight of the subject was also compared with the number of questionnaire responses and a correlation of .28 was found. All of these correlations could have occurred by chance more than 5 times in 100 trials, with the sample size used. This varied with the different measures since not all subjects had taken all tests.

Table 2 gives the average scores of the "low" symptom group and of the "high" symptom group on the different subtests of the Wechsler-Bellevue Intelligence Scale, as well as the average Verbal, Performance, and Full Scale *IQ*'s. The probability that differences between these two groups could have occurred by chance was determined by the Wilcoxon non-parametric technique of unpaired replicates, and appears in the table. The arithmetic subtest was found to differentiate significantly between the "low" and "high" symptom groups at better than the .02 level. The differences between the two groups on the Block Design subtest and the Verbal Scale *IQ* could occur by chance less than 10 times in 100 trials. There is a difference between the two groups on the Performance Scale *IQ*, significant at the .10 level.

While the differences between the "high" and "low" symptom group on the remaining subtests and on the Full Scale *IQ* can occur by chance more than 10 times in 100 trials, it should be noted that the "high" symptom group did better on four of the five tests comprising the Verbal Scale; the "low" symptom group did better on four of the five tests comprising the Performance Scale. The two groups were comparable in their scores on the Similarities and on the Picture Completion tests. The "high" group had a higher

Verbal Scale *IQ* and the "low" group had a higher Performance Scale *IQ*. There was practically no difference between the groups on the Full Scale *IQ*.

TABLE 2

COMPARISON OF "LOW" AND "HIGH" SYMPTOM GROUPS ON WECHSLER-BELLEVUE INTELLIGENCE SCALE SCORES
($N = 6$ in each group)

Item	Average score "Low" symptom group	"High" symptom group	P*
Verbal Scale			
Information	13.3	14.0	—
Comprehension	12.7	13.7	—
Digit Span	10.0	13.3	—
Arithmetic	10.2	15.3	<.02
Similarities	14.5	14.5	—
Performance Scale			
Picture Arrangement	11.3	9.3	—
Picture Completion	11.3	11.0	—
Block Design	14.3	11.8	<.10
Object Assembly	12.0	10.3	—
Digit Symbol	13.8	11.7	—
Verbal Scale IQ	116.8	128.5	<.10
Performance Scale IQ	121.0	108.5	.10
Full Scale IQ	120.5	120.8	—

*P, or probability of chance occurrence of difference between two groups, was determined by the Wilcoxon non-parametric technique of unpaired replicates (12).
— Indicates that P is $> .10$.

The average scores obtained by each group on certain quantitative variables of the Rorschach test and the probability that the differences between the groups would arise by chance appear in Table 3. The Wilcoxon test was applied here, too. A difference which could occur by chance less than .05 times was obtained for the popular response (P) variable, where the "low" symptom group gave a greater number of these responses. The variables, percentage of percepts containing animal plus animal details (A+Ad%), and the number of percepts containing diffuse shading or vista (K) showed differences between the two groups which could have occurred by chance less than 10 times in 100. The "low" symptom group scored higher on the former variable; the "high" symptom group scored higher on the latter variable. The two groups differed significantly (.10 level) in the ratio of human to animal percepts (H:A); a higher ratio was obtained by the "low" response group.

Although the differences on other variables were not statistically significant, that is, could have arisen through chance more than .10 times, it is interesting to note that the average performance of the groups usually

differed. The "high" symptom group scored higher on the following variables: D, S, M, m, FC, CF, ΣC, F%, H+A: Hd+Ad, and W:M. Higher scores were obtained by the "low" symptom group on these variables:

TABLE 3

COMPARISON OF "LOW" AND "HIGH" SYMPTOM GROUPS ON RORSCHACH TEST VARIABLES ($N = 6$ in each group)

	Variables	Average score "Low" symptom group	Average score "High" symptom group	P*
Location				
	W	30.5	27.5	—
	D	59.7	67.3	—
	Dd	10.0	8.5	—
	S	1.3	2.7	—
Determinant				
	M	2.5	3.2	—
	FM	5.8	4.0	—
	m	2.5	5.0	—
	K	0.2	2.5	<.10
	k	1.2	1.2	—
	c	4.8	3.2	—
	C′	2.3	1.8	—
	FC	1.8	2.3	—
	CF	0.7	1.8	—
	C	1.5	1.2	—
	ΣC	3.8	5.3	—
Other				
	R	31.2	32.0	—
	P	9.0	6.7	<.05
	F%	34.3	40.3	—
New	F%	85.8	85.0	—
	F+%	79.5	76.5	—
New	F+%	87.8	86.8	—
	A+Ad%	49.2	33.0	<.10
	H+A:Hd+Ad	33.0	61.3	—
	H:A	675.0	315.7	.10
	M:ΣC	171.7	168.8	—
	FM+m:c+C′	95.8	54.0	—
	R 8-10%	41.7	38.3	—
	W:M	33.3	55.3	—
	M:FM	302.7	175.2	—

*P, or probability of chance occurrence of difference between two groups, was determined by the Wilcoxon non-parametric technique of unpaired replicates (12).
— Indicates that P is $>$ .10.

W, Dd, FM, c, C′, F+%, new F+%, M:ΣC, FM+m: c+C′, R 8-10%, and M:FM. Average scores were fairly comparable on k, C, R, and new F%.

Since N was small, another procedure was introduced to see whether the differences significant at the .10 level or better could be viewed with

greater assurance that they were not due to chance. Accordingly, the "middle" symptom group was compared with the "low" and with the "high" groups and was found to be a middle response group on six of the eight variables studied. The variables K and H:A did not show this relationship.

D. Discussion

The findings point out that a substance such as tap water, which is generally considered chemically and pharmacologically inactive, is capable of eliciting certain responses from certain subjects who believe they have received lysergic acid diethylamide. These observations emphasize once more the need for placebo controls in studies investigating the effects of drugs; without them changes which are produced merely by the situation and not by the drug are frequently falsely attributed to the action of the drug.

The subjects who give many responses under a placebo are frequently called "suggestible." Yet the suggestibility may be attributed to a variety of factors other than those inherent in the subject. In our experiments the results obtained with the two questionnaires were decidedly different. With the first, the number of different responses by the group ranged from zero to 15; with the revised questionnaire the greatest number of positive responses by any one subject was 4. While there were only five subjects tested with the revised questionnaire, and it is possible that none of these subjects are "suggestible," it seems likely that the number of positive responses made is partly a function of the questions asked. The new questionnaire is "tailored" to elicit more significant LSD-25 reactions.

One of the other difficulties of a questionnaire as an instrument for measuring suggestibility is that it does not determine the response threshold of subjects. Subjects who may be equally suggestible, in that they experience the same severity of a symptom, may differ in the degree of change which must be present before they will report this symptom. Furthermore, the responses of other subjects in the group tested together may also influence the responses of the placebo subject. Because of the variable effects produced by different circumstances, the observations concerning the present group of subjects can apply only to their behavior in our specific experiments. We have classified subjects as "low" responders and "high" responders, but we cannot legitimately use these labels for the subjects when they are placed in other settings. Within our framework, however, we can attempt to describe the nature of the responses given to a tap water placebo and the relationship of the responses to other variables.

Most subjects who respond to a placebo tend to do so most markedly during the first ½ hour after receiving the substance. At this time their anticipation of, and anxiety about, the effects of LSD-25 are probably greatest. Gradually the effects wear off, as the anticipation wears off. Individual differences exist in the time of peak effect, but this is the most common finding. The questions which elicited the greatest percentage response from the group were those related to anxiety (moist palms and feeling anxious) or to phenomena which commonly occur without the presence of any foreign agent (drowsiness, fatigue, and headache). The remaining questions received random responses.

The fact that there is a wide range in the number of positive responses made to the questionnaire is of major interest. The problem is to determine what characterized the "low" response group as opposed to the "high" response group. Because of the small number of subjects studied none of the Pearson product-moment correlations are significant at even the .05 level. A responding tendency alone (or lack of it) does not seem to be related to the number of questionnaire responses which will be made since the correlation between the number of positive questionnaire responses and the number of positive responses on the Cornell Medical Index Questionnaire was —.05. Here, too, there were many questions of the same type, i.e., relating to symptoms which required the subject's interpretation before he could respond, but apparently the situations differed for the subject. In the medical questionnaire the subject was answering questions concerning his general state of health, and not his immediate state; he also did not at this moment anticipate receiving a drug whose effects might be those suggested in the questionnaire.

We could predict, with only a slight degree of success, the number of positive responses a subject would make on the questionnaire on the basis of his body weight. We could predict more accurately that the subject who is able to do a greater number of simple numerical computations would probably give a greater number of positive responses on the questionnaire.

In the comparison of the "low" and the "high" symptom groups the "low" showed a significantly greater ability to abstract and synthesize on a performance level, as measured by the Block Design subtest of the Wechsler-Bellevue Intelligence Scale. This group showed a tendency to perform better than the "high" symptom group on all Performance Scale subtests but one (Picture Completion), and had a significantly higher Performance Scale *IQ* than the "high" symptom group. The "high" symptom group, on the other hand, showed a much higher ability to concentrate and solve verbal arithmetic problems, as measured by the arithmetic subtest. With

the exception of the Similarities subtest, the "high" symptom group tended to perform at a higher level on each Verbal Scale test, and in fact had a significantly higher Verbal Scale *IQ*. Thus it appears, from this test, that subjects in the "high" symptom group stress a verbal or ideational approach in their efforts at adaptation, while the "low" symptom group subjects place a stress on motor or performance functions in their adaptive efforts. In addition, on the Rorschach test, the "low" symptom group was found to be much more stereotyped in their thinking and to emphasize the popular and conventional modes of responding. If subjects respond to their environment in the same way that they respond to the Rorschach ink blots then this "low" symptom group may be considered conventional in their responses in other situations.

It seems that it was the ideationally-oriented individuals rather than the primarily action-oriented individuals who demonstrated a greater amount of suggestibility, that is, a greater response, to the placebo in our experiments.

Certain other variables seem to be related to the number of responses made by our subjects. Professionally, there seems to be a difference between the "low" and "high" response groups. Among the seven subjects giving the fewest number of positive responses five of them are in fields where they are probably familiar with experimental techniques and the use of placebos in research. Among the seven giving the greatest number of positive responses only two were in comparable scientific professions. It was also observed that among the first 11 subjects 10 were female, whereas among the last 11, only four were female. What these observations mean is difficult to say.

Lasagna and Von Felsinger (7) reported that the motivation of subjects who volunteer for drug experiments is usually related to their responses. They enumerate three major motives: (*a*) desire for money, (*b*) desire for new experiences, and (*c*) escape from their problems. The motive, together with the subject's personality, may influence the attitude towards the questions and the manner in which subjects respond to them. One of their subjects felt she was not earning her money if she did not show a reaction; some of their subjects seemed to fulfill their need for escape from their problems by giving a large number of responses. Our subjects often appeared to be seeking help in solving their psychological problems.

A high correlation was found between the number of positive responses given under the placebo and the number given under the drug (1). If it is possible to fully understand the type of individual who responds to a placebo then it may be possible to predict how the subject under the influence of LSD-25 will respond to the questionnaire, under comparable circumstances.

In addition to studying the number of responses some additional information about suggestible persons, within this experiment, might be obtained by studying the specific responses made by the "high" response group as compared to the "low" response group.

E. Summary and Conclusions

Thirty-three non-psychotic adults were tested in groups of two to five subjects. They received a placebo of 75 cc of tap-water instead of lysergic acid diethylamide. On the basis of their periodic responses to a questionnaire and comparison of their responses with other variables, certain conclusions can be made under our experimental conditions.

1. Subjects reacted with varying degrees of severity to a placebo. Some gave no positive responses to any question; one subject responded positively to as many as 15 different questions (out of a possible 47), during three time intervals.

2. The most common symptoms reported after 28 subjects received a placebo were, in order of decreasing frequency: moist palms, headache, fatigue, drowsiness, anxiety, illness, dream-like feeling, increased appetite, unsteadiness, hotness, weakness, and heavy feeling in the hands and feet. Presence of these symptoms was indicated by at least 25 per cent of the subjects and as many as 60 per cent for some symptoms. These in general correspond to certain of the symptoms of the LSD-25 reaction.

3. The greatest number of positive responses was given by most subjects within ½ hour after the ingestion of the placebo; the effect tapered off during the next few hours.

4. The number of positive responses a subject made appeared unrelated to his total body weight or to the number of positive responses he made on the Cornell Medical Index Health Questionnaire. A positive relationship between his scores on an arithmetic test and his questionnaire responses was suggested, although the correlation was not statistically significant with the sample size available.

5. Comparison of the subjects giving the least number of positive responses with those giving the greatest number of positive responses to the questionnaire showed that those in the "low" response group tended to be primarily action-oriented in their adaptive efforts, while those in the "high" response group tended to be ideationally-oriented, as suggested by their responses on the Wechsler Bellevue Intelligence Scale. Only some subtests (Arithmetic and Block Design) showed significant differences between the two groups, but the suggested difference was present in 8 of 10 subtests. Thus within our

framework, those who perform better on a verbal level appear more suggestible. The subjects giving an intermediate number of positive responses to the questionnaire also tended to score midway on the Wechsler Bellevue subtests.

6. Those in the "low" response group tended to be more stereotyped in their thinking and emphasized the popular and conventional modes of responding, as suggested by their responses on the Rorschach test.

7. Other variables which may be related to the responding tendency of subjects are: profession, sex, and motivation for participating in experiments.

8. Preliminary data are presented for a revised questionnaire specifically geared to the LSD-25 reaction.

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