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LYSERGIC ACID DIETHYLAMIDE (LSD-25): X. EFFECT ON REACTION TIME TO AUDITORY AND VISUAL STIMULI*

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A. INTRODUCTION

Recent investigations have shown that LSD-25 has deteriorating effects upon such psychological functions as perception (1), memory (7), attention and concentration (6). Rinkel (11) observed "hesitancy and indecision" while Stoll (13) noted "loosening up of thought processes" in subjects under the influence of lysergic acid diethylamide.

The aforementioned processes, as well as other psychological abilities and motor abilities, are probably involved in the usual tests of reaction time. Since LSD-25 disrupts the use of these functions, to a greater or lesser extent, it is plausible that it would also lengthen reaction time.

Research with other drugs has demonstrated that they have variable effects upon reaction time. Benzedrine produces a slight but reliable improvement in complex reaction time to a visual stimulus (5) but has little effect on reaction time to auditory stimuli (14). Small doses of morphine have a diphasic effect, first shortening and then lengthening reaction time (8). Kraepelin has reported a similar phenomenon with alcohol (17, p. 336).

Although inconsistent changes in simple reaction time occur at altitudes above 13,000 feet, there is an increase in complex reaction time (9, 10). An increase in visual reaction time is produced by a 30 per cent saturation of carbon monoxide (2).

The purpose of this study is to determine the effects of lysergic acid diethylamide upon manual and verbal reaction time to auditory and visual stimuli.

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B. Method

1. *Subjects*

The sample was comprised of 12 paid, adult volunteers: six male and six female. Their ages ranged from 21 to 33, with the median at 27 years. Only those volunteers who were considered non-psychotic on the basis of a psychiatric interview and a battery of clinical psychological tests (1) were accepted as subjects. All subjects were at least average in intelligence, as measured by the Wechsler-Bellevue Intelligence Scale, and eight fell in the superior range. Seven of the subjects were graduate students in psychology or allied fields. There were two housewives, an auditor, a hair-dresser, and a public relations worker.

2. *Apparatus and Tests*

An electronic chronoscope recorded in milliseconds the manual reaction time to a given stimulus. Four types of tests were used: simple reaction time to sound, simple reaction time to light, complex uncrossed reaction time to light, and complex crossed reaction time to light (12).

The sound stimulus consisted of a 60-cycle per second vibration transmitted through a set of Telex Monoset earphones. Two 6-volt tungsten filament bulbs with red filters comprised the light stimulus. They were situated 11 *cm* apart on a wooden screen before the subject. There were two telegraph keys, 15 *cm* apart on the table in front of the screen.

In each simple reaction time test there were 10 trials in which the subject released the right telegraph key and 10 in which he released the left key, as soon as he perceived the stimulus. In addition, there were three practice trials given before each series of 10 trials, and two "catch" trials inserted after the third and the seventh trial. In the "catch" trials the experimenter gave the ready signal but omitted the stimulus. This served to prevent automatic responses without regard to the stimulus.

The complex reaction time tests contained 20 trials each and three practice trials. The dichotomous sequence devised by Gellerman (4) was used to determine the order of illumination of the right and left bulb. An automatic programmer utilizing a punched tape controlled the time interval between trials. A chime signified "ready" and the subject depressed the key. The stimulus appeared two seconds later.

In addition to the tests involving manual response to stimuli, the battery included tests of verbal response to a series of visual stimuli, taken from Wells and Ruesch (15). There were two parts: square patches of five com-

mon colors randomly repeated so that there was a total of 50 squares, 10 on a line, and, on the back of this page, names of these colors printed in the same sequence. The five colors or words appeared on the first line and served as a practice trial for the subject. The experimenter timed the subject with a stop watch as he read all of the 50 words, and as he named all of the 50 colors.

3. *Procedure*

a. Administration of drug. The subjects took the drug, diluted in 75 *cc* of tap water, at approximately 9:30 A.M. Groups of three, four, or five subjects took the drug and the tests in an air-conditioned room where the preliminary interviews and the psychological testing had formerly taken place. Two experimenters administered the drug and the reaction time tests.

The tests were administered four times with at least a one-week interval between sessions. The subjects received only 75 *cc* of tap water and no drug at their first session. Since LSD-25 is tasteless, colorless, and odorless the subjects could not detect the amount of drug they had ingested, and the first session served as a control experiment. At the second and third sessions the subjects received 50 micrograms and 100 micrograms of the drug, respectively. The last session was another placebo or zero dose experiment in which only eight subjects participated. The data from this session was used to evaluate the effects of repetition of the tests on the results. During any experiment the doses of the several subjects usually varied.

The subjects had eaten no food since the previous evening. One-half hour after the ingestion of the drug they ate a light breakfast. Neither smoking nor stimulants, such as coffee and tea, were allowed during the entire testing period.

b. Administration of tests. Approximately 2 to 2½ hours after receiving the drug the subjects took the reaction time tests. This interval was within the range when the drug effect is maximum (1). The tests followed approximately a one-hour period during which a variety of group paper and pencil tests were administered. The reaction time tests were individual tests, and during the half-hour period the two experimenters also gave individual pursuit rotor and steadiness tests.

The subject sat before the reaction time apparatus for the manual response test. The following paragraphs give the instructions for each subtest:

> "Each time you hear the chime, press the *right* telegraph key down with your *right* index finger. As soon as you hear the buzzer through the earphones, which you will put on in a moment, let up on the key as quickly as you can. Speed is the important thing here. Now, put

the earphones on, and keep your eyes closed during this test. Do you understand what to do? Ready?"

"Now, you are to follow the same procedure, except that now you will put the *left* telegraph key down with your *left* index finger when you hear the chime, and let up on it when you hear the buzzer. Remember to keep your eyes closed."

"You may take off the earphones now. This time you are to put the *right* key down again each time you hear the chime, and as soon as you see the bulb on the *right* side light up, let up on the key as quickly as you can."

"Now, put the *left* key down when the chime sounds, and let it up as soon as the bulb on the *left* side lights up."

"This time you are to put *both* telegraph keys down when you hear the chime. If the bulb on the *right* side goes on, you are to let up on the *right* key, and if the bulb on the *left* side goes on, let up on the *left* key, again, as quickly as you can."

"Again put *both* keys down when you hear the chime, but this time the procedure will vary a little. If the *left* bulb lights up, let up on the *right* key, and if the *right* bulb lights up, let up on the *left* key. Remember, you are always to let up on the key which is opposite the light that goes on."

Following each set of instructions the corresponding tests followed. There were 13 trials in each of the tests of simple reaction time, and 23 in complex reaction time tests.

The experimenter recorded the reaction time to each stimulus on a prepared form. The data from the first three trials of a series were recorded but were not used in the statistical analysis. The subject did not know that these were practice trials, but if there was any error in his procedure it was corrected during this time.

For the verbal reaction time tests the experimenter held the page of words before the subject and told him to read the top practice line first. After the subject completed this successfully, the experimenter told him to read all the words on the page, reading from left to right, as quickly as he could. Total time in seconds was recorded with a stop watch. The subject then took the color naming test in the same manner.

The same form of the tests was administered at each testing session.

c. Analysis of data. First, the 20 trials in each subtest of the manual response tests were averaged to provide a reaction time representative of each subject. The Wilcoxon technique of paired replicates (16) then served to indicate whether there were significant differences among the three dose groups, compared two at a time. The group results of each test (simple reaction time to sound, simple reaction time to light, complex uncrossed re-

action time to light, complex crossed reaction time to light, color reading, and color naming) were analyzed this way. Averages of the group were also computed.

In order to determine whether practice with the given tests and experience in the test situation would improve performance, the data analysis also included comparisons of the pre-drug placebo with the post-drug placebo average reaction times on each test by means of the Wilcoxon technique. Spearman rank-order correlation coefficients (3) related for each test the rank position of the subject within the group under the three doses, compared two at a time.

C. Results

The mean reaction times of the group on the various tests under pre-drug zero, 50 and 100 micrograms of LSD-25 appear in Figures 1 and 2. Figure

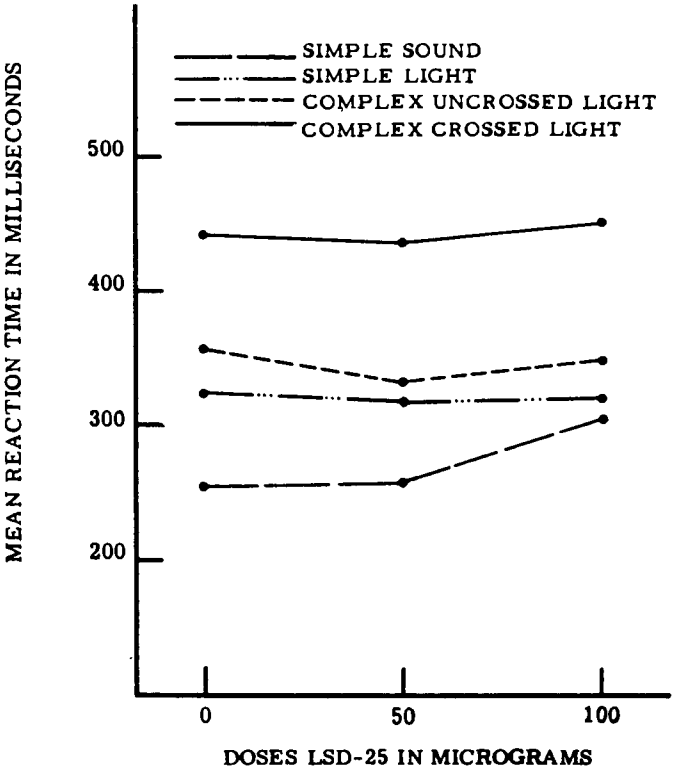

FIGURE 1

Mean reaction time, in milliseconds, to each of four tests of manual reaction time to auditory and visual stimuli. Eleven subjects were tested under zero and two doses of LSD-25.

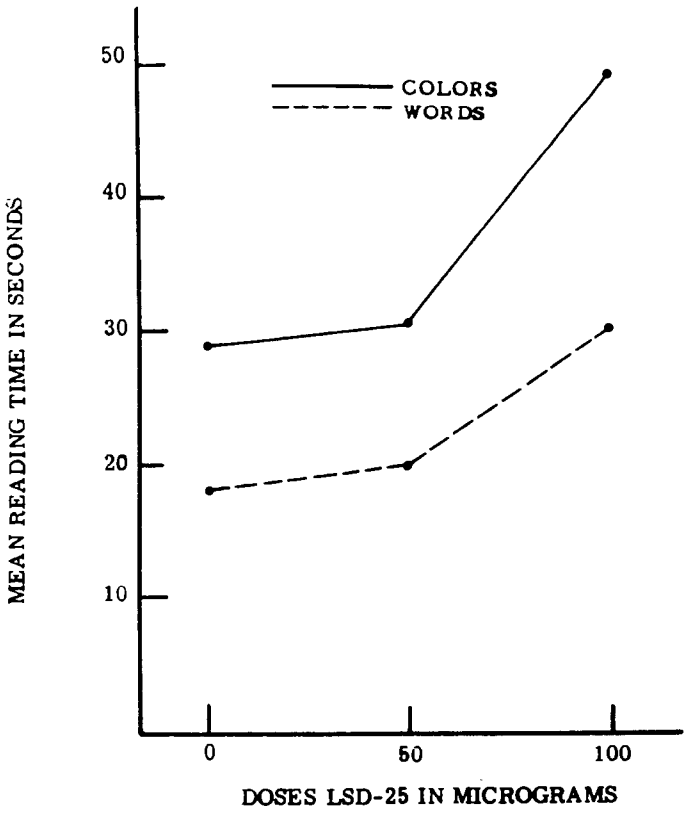

FIGURE 2

Mean reaction time, in seconds, to each of two tests of verbal reaction time to visual stimuli. Twelve subjects were tested under zero and two doses of LSD-25.

1 gives the mean reaction time on manual response tests for an N of 11. One subject did not take the test under 100 micrograms of the drug due to mechanical difficulties. In order to facilitate comparisons among doses her scores were eliminated from the zero and 50 microgram results. No marked consistent changes in the averages occur with increasing dosage. Simple reaction time to light remained almost constant under the three doses. Simple reaction time to sound and complex crossed reaction time to light remained almost the same under 50 micrograms as it was under the pre-drug zero dose. Both increased under 100 micrograms. Complex uncrossed reaction time to light decreased slightly under 50 micrograms and then increased under 100 micrograms to a level between the zero and 50 microgram scores.

The average reaction times on these four tests ranged from about 250 to

+50 milliseconds. Regardless of dose, simple reaction time to sound was always the shortest and complex crossed reaction time the longest. Simple reaction time to light and complex uncrossed reaction time to light fell between these two: the simple reaction time was the shorter.

Table 1 indicates the probability of chance occurrence of differences between scores under the three doses, compared two at a time. The only difference which was significant at the .05 level was that between the pre-

TABLE 1

PROBABILITY OF CHANCE OCCURRENCE OF DIFFERENCES BETWEEN SCORES
(Comparison of Two Doses of LSD-25 and Two Controls)

	Doses LSD-25 Compared			
Test	Pre-drug zero vs. 50 micrograms	Pre-drug zero vs. 100 micrograms	50 micrograms vs. 100 micrograms	Pre-drug zero vs. Post-drug zero
*Manual**				
Simple Sound	—	.05	—	.02†
Simple Light	—	—	—	.01†
Complex Uncrossed Light	—	—	—	.02†
Complex Crossed Light	—	—	—	.01†
*Verbal***				
Colors	—	.02	<.01	.05†
Words	.02	<.01	—	—†

Notes:
— indicates that probability of chance occurrence is greater than .05.
* $N = 11$.
** $N = 12$.
† $N = 8$.

drug zero and the 100 microgram scores on the test of simple reaction time to sound. All other differences could have occurred by chance more than five times in 100 trials.

The results of the verbal response tests appear in Figure 2. The mean total reading time of the 12 subjects is plotted in seconds for each of the tests under the first three doses. There was a progressive increase in average total time with increasing dosage. The increase between zero and 50 micrograms was slight when compared to the much larger increase from 50 to 100 micrograms of LSD-25. The total times ranged from about 18 seconds to about 50 seconds. Reading the words always took less time than naming the colors.

Table 1 also reports the probability that the differences among the various doses in total time to read and name colors, would have occurred by

chance. For the naming of colors the slight increase from the zero to the 50 microgram score could have occurred by chance more than five times in 100. The difference between zero and 100 micrograms was significant at the .02 level; that between 50 and 100 micrograms was significant at better than the .01 level.

On the test of word reading the increase between the zero and the 50 microgram scores was significant at the .02 level and the increase between zero and 100 micrograms was significant at better than the .01 level. The increase between 50 and 100 micrograms could have occurred by chance more than five times in 100.

Comparison of scores obtained under the pre-LSD-25 placebo with those obtained under the post-LSD-25 placebo yielded results which are summarized in Figures 3 and 4, and Table 1. Only eight subjects took the sec-

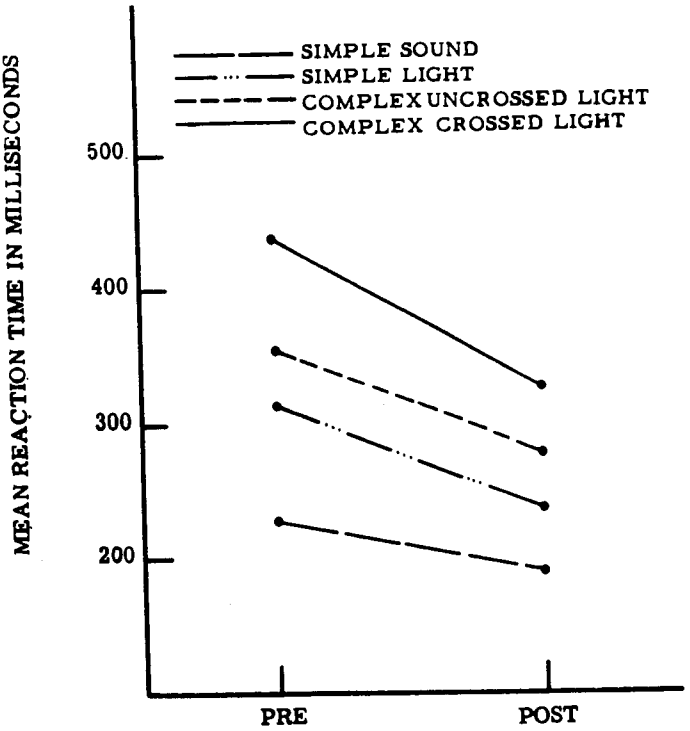

FIGURE 3

Mean reaction time, in milliseconds, to each of four tests of manual reaction time to auditory and visual stimuli. Eight subjects were tested under zero doses of LSD-25, before and after drug tests.

ond zero dose. The mean reaction times of these eight subjects on the manual response tests appear in Figure 3. All four tests showed decreased average reaction time under the second placebo. The order among the tests remained the same as under the first placebo. Figure 4 shows the means of the

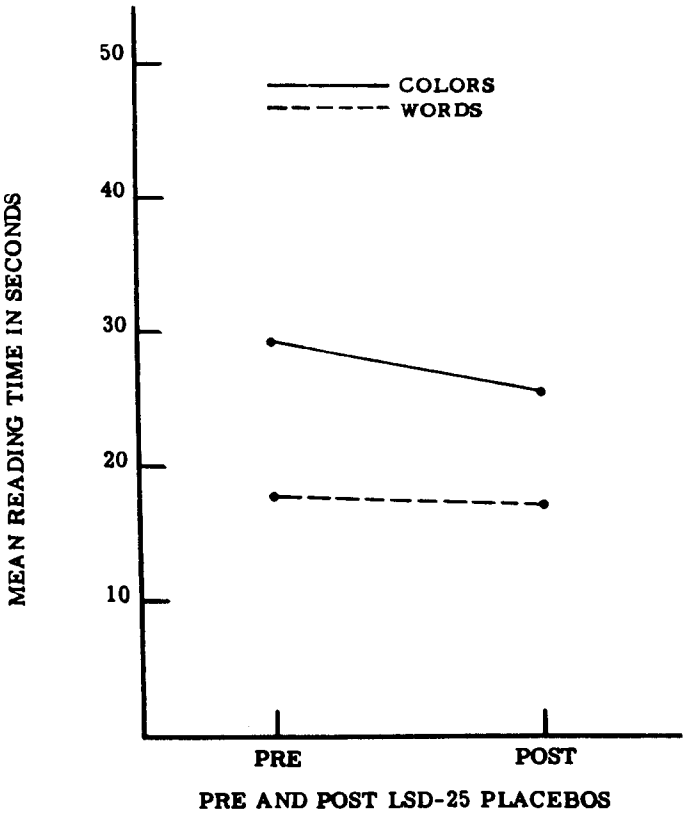

FIGURE 4

Mean reaction time, in seconds, to each of two tests of verbal reaction to visual stimuli. Eight subjects were tested under zero doses of LSD-25 before and after drug tests.

verbal response tests. Both of these average times were shorter under the second placebo.

Table 1 indicates that all the improvements on the manual response tests were significant at the .02 level or better. The improvement in the naming of colors was significant at the .05 level. Only the decrease in time to read the color names could have occurred by chance more than five times in 100.

The data presented in Table 2 show the rank-order correlation coefficients relating the subject's rank position under one dose to his rank position under another dose, for each of the six reaction time tests. All three dose groups

TABLE 2
SPEARMAN RANK-ORDER CORRELATION COEFFICIENTS RELATING REACTION TIMES
(Three Doses Related, Two at a Time)

	Doses LSD-25 Compared					
	Pre-drug zero vs. 50 micrograms		Pre-drug-zero vs. 100 micrograms		50 micrograms vs. 100 micrograms	
Test	ρ	P	ρ	P	ρ	P
*Manual**						
Simple Sound	.36**	—	.37	—	.14	—
Simple Light	.33**	—	.73	.01	.33	—
Complex Uncrossed Light	.23**	—	—.07	—	.76	<.01
Complex Crossed Light	.43**	—	.33	—	.62	<.05
*Verbal***						
Colors	.78	<.01	.41	—	.76	<.01
Words	.62	<.05	.40	—	.82	<.01

Notes:
ρ is the Spearman rank-order correlation coefficient.
P is the probability of chance occurrence of the correlation coefficients.
— indicates that P is > .05.
* $N = 11$.
** $N = 12$.

were compared, two at a time. The probability that each coefficient would have occurred by chance, with the given N also appears in the table. A high coefficient means high correspondence between ranks; a low coefficient means little correspondence. Among the manual response tests only three of the 12 correlation coefficients were as high as .62 and significantly differed from zero. One of these correlations related the rank position under zero and 100 micrograms LSD-25 on the test of simple reaction time to light, another the rank positions under 50 and 100 micrograms of the drug on the tests of complex crossed reaction time to light, and the third related the rank positions under 50 and 100 micrograms on tests of uncrossed reaction time to light. All other correlations were .43 or less and could have occurred by chance more than five out of 100 trials. Each verbal response test correlated significantly when the rank positions under zero and 50 micrograms were compared and when those under 50 and 100 micrograms were compared. These correlations ranged from .62 to .82. Correlations between the zero and 100 microgram results were low and not significant for an N of 12.

D. Discussion

The results obtained seem to depend upon the particular stimulus used to measure reaction time. While the manual and the verbal tests both measure the time required for a subject to respond to a stimulus, the processes involved in each are apparently different. In one case the stimulus is a simple light or a simple sound, whereas in the other the stimulus is a complex symbol. In one case the response consists in simply releasing a telegraph key, whereas in the other it consists in making a complex verbal response. Thus, in the former, adequate control over the hands was necessary and in the latter the subject required facility in speaking.

Only one comparison of the manual response test, that between zero and 100 micrograms of LSD-25 on the test of reaction time to sound, showed a significant impairment under the drug. The remaining tests of individual reaction time showed only random changes which were not significant. The data from each subject demonstrated that some subjects consistently improved their average reaction time on successive administrations of the tests, despite the presence of a drug the second and third time. Other subjects showed impairment correlated in amount with the dose of the drug.

Since each subject had 20 trials on each subtest further statistical analysis of the data would show whether the changes in each subject's performance were significant. It appears that lysergic acid diethylamide has different effects upon different subjects.

The reaction time to colors and words seems to be a more sensitive test for detecting the presence of LSD-25. This test may be more difficult since there are five possible stimuli which the subject can receive, as compared with one or two in the manual tests. This explanation is, however, difficult to reconcile with the fact that the one manual test which showed a significant change was the one considered most simple, namely, reaction time to sound. It is possibly more plausible to explain the difference between the two types of tests on the basis of the kind of response made. In the individual reaction time the subject simply indicates with his hand(s) that he perceived the stimulus. In the verbal tests the subject does more than indicate that he perceived the stimulus; he must translate what he sees into a verbal expression, which varies throughout the test. The ability to verbalize and to respond to successively different stimuli undergoes greater impairment under LSD-25 than manual reaction time. This explanation supports the findings that subjects under the influence of LSD-25 exhibit slowness and poverty of speech (11). In addition, visual difficulties and inability to focus

properly may extend the reaction time to the words and colors, under the drug.

It was pointed out that some subjects improved and some deteriorated in performance on the manual response tests, so that the average change was very little. There was a significant improvement on the second zero test scores as compared to the first. Apparently those subjects who had improved regardless of the drug also improved under a second placebo and those who were impaired under the drug improved when the drug was not present to interfere. In the verbal response tests there was a significant improvement under the second placebo on the naming of colors but not the reading of words. Subjects probably had considerable experience in reading names of colors and so their first performance in these experiments was at a high plateau-like level. Translating the perception of a color into the name of that color was most likely a much less familiar process and therefore there was a greater likelihood that subjects would improve under subsequent testing without a drug.

The correlation coefficients relating a subject's performance under one dose with his performance under another, show on the verbal response reaction time tests that it is possible to predict a subject's rank position under one dose from his rank position under another dose with an acceptable degree of success. This can be done between zero and 50 micrograms and between 50 and 100 micrograms. The possibilities here are either that LSD-25 has very little effect on a very reliable test and the subjects keep their same scores with or without LSD-25, or that LSD-25 has the same relative effect on a reliable test. The latter possibility seems to be the actual one, since we have shown (see Figure 2) that LSD-25 *does* have an effect on the test.

On the other hand, the results on the manual response reaction time tests do not show a high rank-order correlation between doses. The possibilities here are that either the LSD-25 had a disruptive effect or affected the subjects differentially; or else, the test was unreliable to begin with.

E. Summary and Conclusions

Twelve non-psychotic subjects were given tests of manual and verbal reaction time under 50 and 100 micrograms of lysergic acid diethylamide and two zero dose placebos. One was given at the first experiment and the second after the two drug sessions. The manual reaction time tests were: simple reaction time to sound, simple reaction time to light, complex uncrossed reaction time to light, and complex crossed reaction time to light. In these tests subjects responded by releasing a telegraph key as soon as they per-

ceived the stimulus. The verbal reaction time tests were tests in which subjects had to read a series of 50 words naming common colors, and give the colors of a series of square colored patches. The following tentative conclusions were made:

1. On the average the manual reaction time tests were not sensitive to LSD-25. The most sensitive one was reaction time to sound, which was significantly impaired under 100 micrograms of the drug as compared to zero. There was a significant decrease in reaction time on all four tests under the second placebo as compared to the first. Prediction of the rank-order of subjects under one dose from the rank-order under another dose cannot be done with any acceptable degree of success.

2. The verbal reaction time tests were sensitive to lysergic acid diethylamide. There were significant score impairments between zero and 50 micrograms and between zero and 100 micrograms in the time to read the words. Time to name the colors increased significantly between zero and 100 micrograms, and between 50 and 100 micrograms. The higher the dose the longer the reaction time. The reaction time for naming of colors significantly decreased on the second placebo testing, as compared to the first. There was a slight, but not significant decrease in reading the words.

There were significant rank-order correlations between zero and 50 micrograms and between 50 and 100 micrograms LSD-25.

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