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LYSERGIC ACID DIETHYLAMIDE (LSD-25): VIII. EFFECT ON ARITHMETIC TEST PERFORMANCE*

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A. INTRODUCTION

Adult subjects under the influence of lysergic acid diethylamide have exhibited hesitancy, indecision, and impaired abstract thinking according to clinical observations. For example, Rinkel *et al.* (12) emphasized these changes. Others (3, 13, 14) have observed increased distractibility and difficulty in concentrating in lysergized subjects. By means of simple cancellation tests and short memory tests the present investigators have quantitatively demonstrated that subjects under the drug are not able to concentrate and remember as well as in their non-drug state (7, 8). It seemed likely that drugs would affect performance on solutions of simple arithmetic problems, if they would affect any of the functions involved in the solution of these problems. These include a complex of many intellectual variables, including attention, concentration, old memory, and new memory.

Altitudes of 13,000 feet or greater have impaired performance on simple addition and subtraction problems (5, 10, 11). Studies with tobacco show an increase in errors with smoking on addition and multiplication problems with no clear-cut effect on speed (2). Another study (6) reported a loss of speed in the case of non-smokers and a gain for smokers in doing continuous mental addition. Unpublished results obtained in this laboratory (9) on the influence of LSD-25 on the Wechsler-Bellevue Intelligence Scale indicate a significant impairment on the arithmetic subtest which involves solution of verbal arithmetical problems.

It is the purpose of this paper to investigate the influence of lysergic acid diethylamide on the solution of simple combinations of addition and subtraction problems, and to discover whether there is a change in performance from one dose level of LSD-25 to another.

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B. Method

1. *Subjects*

The subjects in this study were six male and six female, adult, paid volunteers who were considered non-psychotic on the basis of a psychiatric interview and a battery of clinical psychological tests. Intelligence of the subjects, as measured by the Wechsler-Bellevue Intelligence Scale, ranged from average to superior intelligence. The median age was 27, ranging from 21 to 33. Median weight was 135 pounds, ranging from 103-175 pounds. Seven subjects were graduate students in psychology or allied fields; two were housewives, one an auditor, one a hair-dresser, and one a public relations worker.

2. *Tests*

The test form used consisted of a printed sheet of 400 arithmetic problems.[2] Each problem consisted of three numbers and two operations. Either all three were to be added or two were to be added and the third subtracted. The sheet on which the problems were printed was divided into eight sections of 50 problems each. These eight sections were then arbitrarily divided into four sections providing four comparable forms, each of which had an *"A"* and a *"B"* section.

3. *Procedure*

a. Administration of drug. The drug was administered orally in 75 cc of water at approximately 9:30 a.m. to subjects who had eaten no food since the previous evening. Groups of three, four, or five subjects were given the drug and tested in an air-conditioned room. All subjects had previously been in this room and had met the experimenters during the preliminary interviews and the clinical psychological tests. They sometimes were acquainted with the other members of the group. There were usually four experimenters present in the laboratory, two of whom administered the arithmetic test.

The tests were administered four times with at least a one-week interval between sessions. The first time the subject was tested he was given only 75 cc of water and a zero dose of the drug (a placebo). The second and third time the subject received 50 and 100 micrograms of LSD-25, respectively. To evaluate the effects of repetition of the tests the last session was again a zero dose experiment. Since the drug has no taste, color, or odor the subject had no knowledge of the amount of drug he received. The subjects being tested in any one day usually received different doses.

[2]The authors wish to thank Dr. Hans Werner-Wendt of Wesleyan University, Middletown, Connecticut, for supplying a sample sheet of arithmetic problems.

Half an hour after ingestion of the drug, the subjects received a light breakfast. No stimulants, such as coffee or tea, were permitted and smoking was not allowed during the entire test period.

b. Administration of tests. Approximately 1½ hours after receiving the drug, the subjects took the arithmetic test. Previous to this test the subjects had spent about ½ hour taking tests measuring their memory span on a series of nine different tests (8) and their speed in a series of eight cancellation tests (7). The tests were given during this time since it was shown that maximum effect occurs about 1 to 2½ hours after the drug ingestion (1). The following instructions were given:

> You are now going to take an arithmetic test. When I give you the signal, begin doing the problems in Section *A*. Do only the problems in that section, and stop working when the alarm rings. Work as quickly as you can without making any mistakes.

The subjects did as many problems as they could in a one-minute period. They were then given the following instructions:

> Now, do the test below the one you just did, Section *B*, stopping when you hear the alarm. Do this in the same way in which you did Section *A*.

One minute was allotted for the problems in Section *B*. Each time subjects were tested they were given a different form of the test to minimize practice effects. An attempt was made to use each form with equal frequency at each dose level.

c. Analysis of data. The number of problems solved correctly and the number of errors, on Parts *A* and *B* independently, were tallied. The test score was the number of correct solutions. The scores of pre-drug zero and 50 micrograms of LSD-25, pre-drug zero and 100 micrograms of the drug, and 50 and 100 micrograms were then compared by means of the Wilcoxon non-parametric test of paired replicates (15), to determine whether the score differences between doses were significant.

In order to evaluate the effects of repetition with the given test, the scores obtained under the first zero testing and the second zero testing were compared by the same technique. The Spearman technique of rank-order correlation (4) was used to estimate the predictability of the rank position of a subject under one dose from his rank under another dose of the drug or placebo.

C. Results

The mean number of correct solutions given under three doses of LSD-25 is graphed in Figure 1. Scores decreased, on the average, from an initially high level under zero micrograms of the drug to a lower level under 50

micrograms, and under a 100 microgram dose the average scores were lowest. The Form *B* scores were always slightly lower than those of Form *A*, also decreasing with increasing dosage.

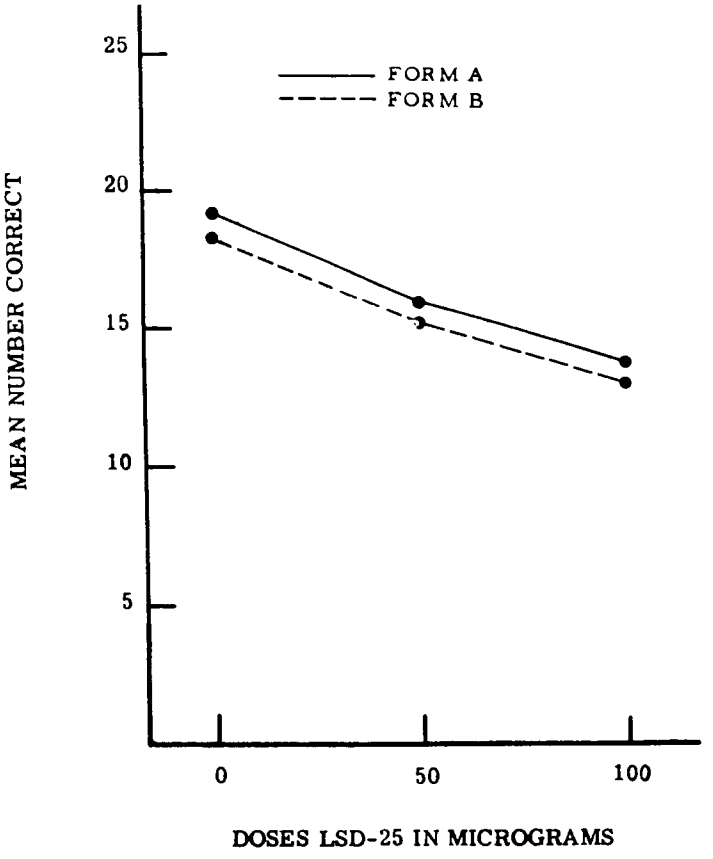

FIGURE 1

Mean number of correct solutions of simple arithmetic problems by 12 subjects tested under zero and two doses of LSD-25

The average number of errors was less than .50 in all three dose groups. There was no significant difference among the groups as tested with the Wilcoxon technique.

Table 1 indicates the probability that the score differences among the three dose levels, taken two at a time, would have occurred by chance. The drop in score from the pre-drug zero to the 50 microgram dose would have occurred by chance less than five times in 100 for Form *A* and Form *B*. Be-

TABLE 1
SCORE COMPARISONS AMONG LSD-25 AND PLACEBO DOSES
(Probability of Chance Occurrence of Differences; Relationship Among Scores)
$N = 12$

	Compared microgram doses of LSD-25							
	Zero versus 50		Zeros versus 100		50 versus 100		Pre-drug Zero versus Post-drug Zero	
	A	B	A	B	A	B	A	B
Probability of differences occurring by chance*	<.05	<.05	<.01	<.01	>.05	<.05	.05**	.02**
(ρ) Rank order correlation	.69	.67	.51	.44	.58	.65		
(P) Probability of correlation occurring by chance	<.05	<.05	>.05	>.05	<.05	<.05		

*Performance was impaired under successively higher drug doses. It improved on the second zero as compared to the first.
**$N = 8$.

tween zero and 100 micrograms a difference significant at better than the .01 level was obtained for both forms. In comparing the scores under 50 micrograms with those under 100 the difference for Form *A* was not significant but that for Form *B* was significant at better than the .05 level.

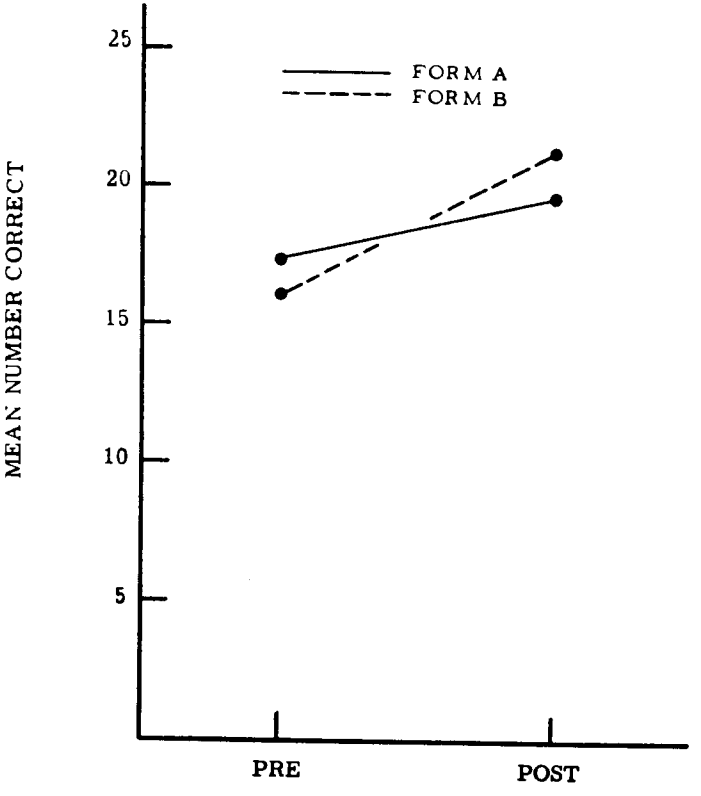

FIGURE 2
Mean number of correct solutions of simple arithmetic problems by eight subjects tested under zero dose LSD-25 before drug tests and after drug tests

In Figure 2 the results of the pre-drug zero and post-drug zero are compared. The probability of chance occurrence of the differences appears in Table 1. For eight subjects who were available for retesting under a zero dose the mean increased from 17.4 on the first testing with Form *A* to 19.8 on the second testing. The increase is significant at the .05 level. Com-

parison of results on Form *B* demonstrates an average increase, significant at the .02 level, from 16.1 to 20.4 correct solutions.

Table 1 also gives the rank-order correlations among the scores under the first three doses, compared two at a time. For an *N* of 12, correlations between the pre-drug zero and 50 microgram scores and between the 50 and 100 microgram scores were significant at better than the .05 level, for Forms *A* and *B*. These coefficients ranged from .58 to .69. The correlations between pre-drug zero and 100 micrograms were lower and could have occurred by chance more than five times in 100, with the *N* used.

D. Discussion

The comparisons among the first three doses become more significant when interpreted in relation to the pre- and post-drug zero sessions. The fact that subjects showed a significant improvement between pre-drug zero and post-drug zero testings indicates that factors which might have operated the first time (such as unfamiliarity with the test, anxiety about the new drug situation, etc.) were present to a lesser extent when the subjects took the last tests. This suggests that if no drug had been given, the two intermediary testings would very likely have shown a progressively increasing number of correct responses. If we knew the effect of practice on this test and could factor it out, then the decrement which appears with increasing drug doses would be even greater and more significant than at present.

The decrease in score on Form *B* in relation to Form *A* on the first three testing sessions was slight when compared to the changes among the various doses. It is interesting, however, that on the second zero dose testing Form *B* scores were higher.

A high rank-order correlation indicates that a subject's position relative to others in the group is similar in two categories which are compared. This type of statistic is unaffected by changes in either the average score or the variability of the group. What it emphasizes is the relationship of members of the group to one another. The data of this experiment show that the highest correlation existed between pre-drug zero and 50 microgram scores. This indicates that LSD-25 tends to disrupt the correlation. The widest discrepancy in rank-order under two doses occurred between zero and 100 micrograms, the two groups which are most different from each other in dose. Thus, higher doses of LSD-25 disrupt the correlation even more than the lower doses.

In order to assess the exact effect of LSD-25 it is necessary to evaluate the mechanisms involved in performance of these simple arithmetic problems.

The subject must not only manipulate numbers in performing the first operation, but he must remember this result for use in executing the second operation. In addition, he must maintain the early formed concept of numbers.[3] The solution of simple arithmetic problems probably demands ability to do abstract thinking, to concentrate and shut out distractions, and to recall numbers. The arithmetic test used in this study appears to be one of the more sensitive tests used by us for detecting the presence of LSD-25, since it was most consistently and most significantly impaired. As a single test it further supports the findings that lysergic acid diethylamide impairs abstract thinking (12), the ability to concentrate (7), and the ability to recall (8) in "normal" adults.

E. Summary and Conclusions

On the basis of 12 non-psychotic adults who were tested under 50 microgram doses of lysergic acid diethylamide, under 100 microgram doses, and under zero doses both before and after the LSD-25 tests with two forms of simple arithmetic problems, the following conclusions can be made:

1. Scores on the tests varied inversely with the drug dose, i.e., the higher the dose, the lower the score.
2. Scores under the various doses were significantly different from each other in five of the six comparisons made. Only the difference between 50 and 100 micrograms on Form *A* could have occurred by chance more than five times in 100 trials.
3. There was no significant difference in the number of errors made under the several doses of LSD-25.
4. There was a significant practice effect between the first time subjects were tested under a zero dose and the second time they were tested under a zero dose. The latter testing followed the 50 microgram and 100 microgram tests.
5. There was a significant rank-order correlation between zero and 50, and between 50 and 100 micrograms LSD-25 test scores but no significant correlation between zero and 100 micrograms LSD-25 test scores.

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[3]One subject commented that "While under the higher dose of the drug, I found that the numbers in the problems were completely meaningless and as a result, I was unable to carry out the designated operation."

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