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LYSERGIC ACID DIETHYLAMIDE (LSD-25): VI. EFFECT UPON RECALL AND RECOGNITION OF VARIOUS STIMULI*

Departments of Medicine, Neurology, and Psychiatry, The Mount Sinai Hospital, New York City

M. E. JARVIK, H. A. ABRAMSON, AND M. W. HIRSCH[1]

A. INTRODUCTION

Previous studies by the present authors (1) upon physiological effects of LSD-25 suggested that there would be some interference in the normal integrative processes of the nervous system which might affect the factors of acquisition and retention. Consequently, in this study, a series of memory tests of varying difficulty, some auditory and some visual, were presented to the same subjects.

Only two studies in the literature have attempted to objectively measure memory changes induced by LSD-25. Sloane (7) reports slight but insignificant decreases on the Wechsler-Bellevue Memory Scale in his group of "healthy controls," schizophrenics, and depressives. He found no significant decreases in the accuracy of recall of a name, address, and message five minutes after learning. He also reported that digit span showed no significant change in any group. Savage (6) reported that there was no impairment of memory as measured by the Wechsler-Bellevue Intelligence Scale. In this laboratory unpublished studies with the Wechsler-Bellevue Intelligence Scale show that under the drug there were significant changes in all memory tests with the single exception of the digit span test.

It is the purpose of this study to investigate the effects of two doses of LSD-25 and a placebo upon the recognition and recall of verbal and visual stimuli. The effects of practice in taking the tests will also be analyzed and the relationship between a subject's performance under a placebo and under the drug will be determined.

B. METHOD

1. *Subjects*

The subjects were 12 paid, adult volunteers, six of whom were male and six female. Only those who were considered non-psychotic on the basis of

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a psychiatric interview and who were believed non-psychotic according to a battery of clinical psychological tests (1) were accepted.

The median age was 27 years, ranging from 21 to 33. The group was at least of average intelligence and eight subjects were in the superior intelligence range, on the Wechsler-Bellevue Intelligence Scale. Seven subjects were graduate students in psychology or allied fields, two were housewives, one an auditor, one a hairdresser, and one a public relations worker.

2. *Apparatus and Tests*

a. Variety. Five visual and four auditory tests were used, containing stimuli of varying degrees of familiarity. Visual stimuli were projected on a screen approximately 6 to 10 feet from the subjects by means of an SVE slide projector with an Airequipt Slide Changer. Tests of this kind were object recall, word opposite recall, nonsense syllable recall, nonsense syllable recognition, and letter recognition. The auditory tests, which were presented verbally by the experimenter, included digit span, sentence recall, unrelated word recall, and paired associate recall.

b. Source and description. Several of the tests were selected from Wells and Ruesch Mental Examiner's Handbook (10), namely: objects, word opposites, and digit span. The object test contained 10 slides each with a line drawing of a simple common object. For word opposites, 10 words, all of which had common antonyms, were projected one at a time. The digit span consisted of a series of four to nine numbers.

Ten nonsense syllables of low association value, as prepared by Melton and Malmo (4) were used for nonsense syllable recall. Five of these together with five other syllables of low association value were arranged in random order to make up the nonsense syllable recognition test.

The letter recognition test consisted of a series of 10 letters, randomly selected from a page of print and presented on a single slide. No two letters were repeated. Ten additional slides contained one letter each, five of which were taken from the original 10 and were randomly arranged among five "new" letters.

Five couplets (in iambic pentameter) randomly selected from Shakespeare's *Romeo and Juliet* comprised the material for sentence recall. Thus, the subjects received 10 lines of 10 syllables each.

Ten unrelated words of comparable frequency of use in the English language were randomly selected from Thorndike (8). The paired associate test contained 10 pairs of words of varying degrees of relatedness and were taken from Melton and Safier (4).

Six equivalent but different forms of each test were prepared.

3. *Procedure*

a. Administration of drug. The drug was administered orally in 75 cc of tap water at approximately 9:30 a.m. Subjects ate no food since the previous evening; one-half hour after the ingestion of the drug they were given a light breakfast. No stimulants were permitted and smoking was not allowed during the testing day.

All 12 subjects were tested three times and eight participated in a fourth session. The dose given to all subjects at their first session was 75 cc of tap water, only. Since LSD-25 is a colorless, odorless, and tasteless substance, the water placebo served as a control for the test situation. Fifty micrograms of LSD-25 were given at the second session and 100 micrograms of LSD-25 at the third. For the fourth session subjects were again given a placebo of tap water. There was an interlude of at least one week between sessions.

Practice, anxiety, and other factors which might influence the test results were not controlled by the more usual experimental design of balanced order. The action of the drug upon a given individual is rather variable and not yet predictable, so it seemed inadvisable to begin with a high dose. The scores obtained under the second placebo served as indices of the effects of practice.

Both the drug administration and testing took place in an air-conditioned room where the subjects were tested in groups of 3, 4, or 5. The doses in any one day usually varied among subjects. The subjects had already been in the room and had met the experimenters during their preliminary interviews and psychological testing. They were sometimes acquainted with the other members of the experimental group.

b. Administration of tests. It was shown that LSD-25 begins to take effect about one-half hour after ingestion and evokes a maximum effect between one and 2½ hours, depending on the dose (1). Thus, one hour after ingestion of the drug the series of memory tests was administered for approximately 15 minutes. Visual tests were presented first. Slides were projected for one second with one second pause between slides except for the recognition tests when the pause was long enough for the subject to write a "yes" or "no" response. Following the 10 slides of the recall tests the subjects had to write down as many items as they could.

The auditory tests followed. Stimuli were read in a monotone by the experimenter at the rate of one per second. Sentences were read in couplets, and the subjects then wrote what they recalled. After each series of digits, and after the 10 unrelated words subjects recalled and wrote whatever they

remembered. After learning the series of 10 paired words, the subjects were given the 10 words randomly rearranged, one at a time, and after each had to try to write the word originally paired with it.

Each time the subject was tested, a different form of the test was used. In a given testing day only one form was administered.

c. Analysis of data. The Wilcoxon non-parametric test of paired replicates (9) was used to test the hypothesis that the group under one dose of LSD-25 responds differently than under another dose. Test scores on the recall tests were the number of correct responses; on the recognition test, scores were the number of correct minus the number of incorrect responses. Comparisons were made between the placebo and 50 microgram, between the placebo and 100 microgram, and between the 50 and 100 microgram sessions.

The same method was used to compare the two placebo testings to determine whether there was a difference in performance. Unlike the familiar *t* test the use of this technique does not require the assumption of a normally distributed population. Relationship between performance under two doses was determined by a Spearman rank-order correlation coefficient (3).

C. Results

The results are shown in Figures 1 through 4 and Tables 1 and 2. The mean scores obtained by the group of 12 on the visual memory tests under three doses of LSD-25 are given in Figure 1. For the most part, the scores decreased from an initially high value at zero micrograms to a lower value at 50 micrograms of LSD-25, and to a still lower value at 100 micrograms. Exceptions were the word opposite test where there was a slight increase from the zero to the 50 microgram score, and the nonsense syllable recognition where there was no score change between the 50 and 100 microgram level. In general, the highest scores were obtained on the recognition tests, and the lowest on the recall of nonsense syllables.

The mean scores under the three doses on the auditory tests, as seen in Figure 2, indicate that only two of the tests showed consistent score decrease with dose increase: sentences and unrelated words. Under 50 micrograms of LSD-25 paired associate scores showed an increase followed by a decrease under the next higher dose. The digit span increased very slightly under 50 micrograms and remained at that level under 100 micrograms.

The probability that the score differences between doses are due to chance fluctuations is given in Table 1. Only some of the observed changes in score were significant. Recall of nonsense syllables showed the greatest percentage

change and was among those tests whose differences were most significant. Digit span, on the other hand, was affected little, if at all, by LSD-25, with a very slight increase in scores on successive testings. The number of correct

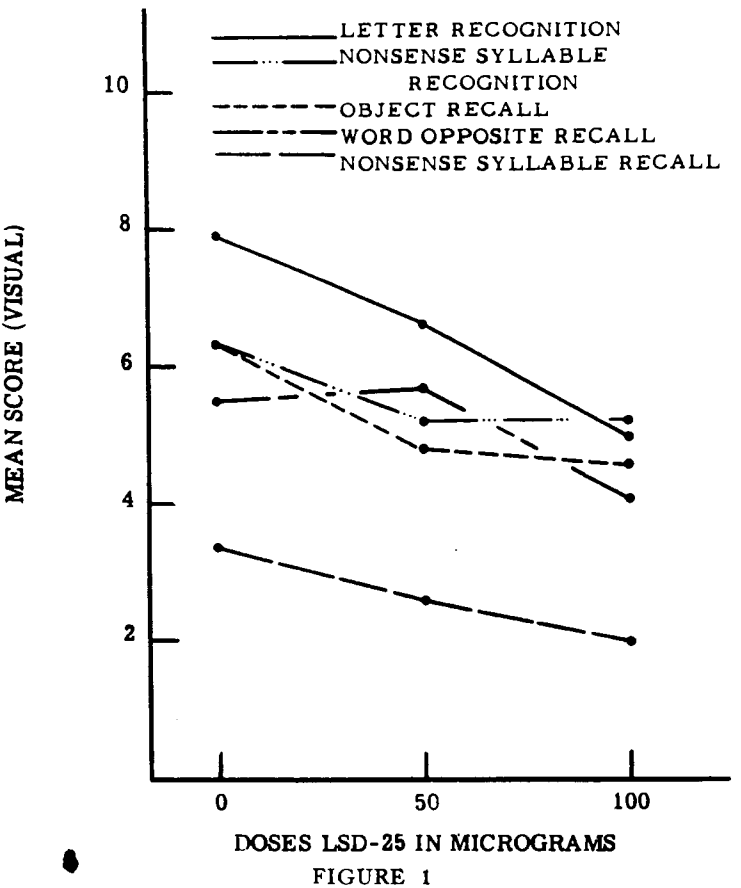

FIGURE 1

Mean number of correct memories on 5 visual recall and recognition tests. Twelve subjects were tested under zero and two doses of LSD-25.

items in each test tended to decrease with increasing dosage, and the number of errors made tended to increase with the dosage increase. Letter recognition, nonsense syllable recall and recognition, paired associate recall, and sentence recall best illustrated this phenomenon. The only increase in errors which was significant at the .05 level or better was that between zero and 100 micrograms on the letter recognition test.

In Figures 3 and 4 the effects of repeated experience with the test are

summarized. Eight subjects were studied. The scores on the first placebo and on the second placebo testing are called pre- and post-LSD-25 placebos, respectively. All the visual and auditory tests showed improvement on suc-

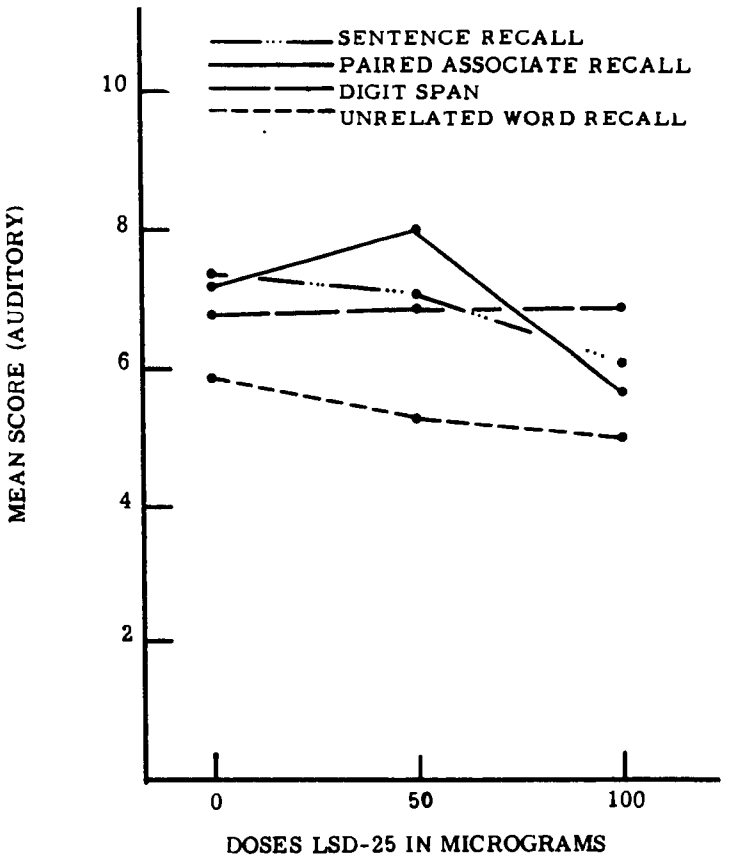

FIGURE 2

Mean number of correct memories on 5 auditory recall and recognition tests. Twelve subjects were tested under zero and two doses of LSD-25.

cessive testings. The second time that subjects received a placebo, with one exception, the scores were the highest of the four experimental days. (Paired associate scores were highest under a 100 microgram dose.) The sentence recall improvement was significant at the .02 level. The changes in performance on the other tests could have occurred by chance more than five times in 100 trials with an N of eight.

The Spearman rank-order correlations, comparing for each test the sub-

ject's rank position within the group under different doses, are given in Table 2. No significant correlations were found for letter recognition, object recall, and word opposite recall. Nonsense syllable recognition, nonsense syl-

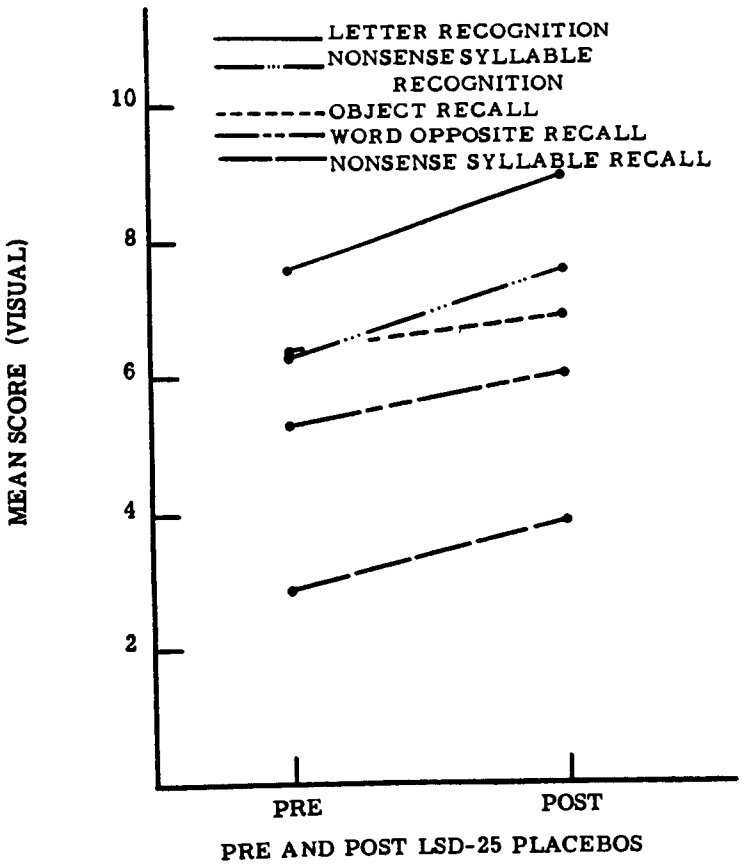

FIGURE 3

Mean number of correct memories on 5 visual recall and recognition tests. Eight subjects were tested under zero dose LSD-25 before and after drug tests.

lable recall, and unrelated word recall showed significant correlations of at least .74 between the two LSD-25 doses. Sentence recall ranks correlated significantly between zero and 100 micrograms and between 50 and 100 micrograms; digit span between zero and 50, and between 50 and 100 micrograms. A significant correlation was obtained for the recall of paired associates between zero and 100 micrograms of the drug.

D. Discussion

The results show that LSD-25 has a deleterious effect upon the learning of various kinds of visual and auditory stimuli. The situation is reminiscent of the findings of Elliot (2) on latent learning where learning or practice

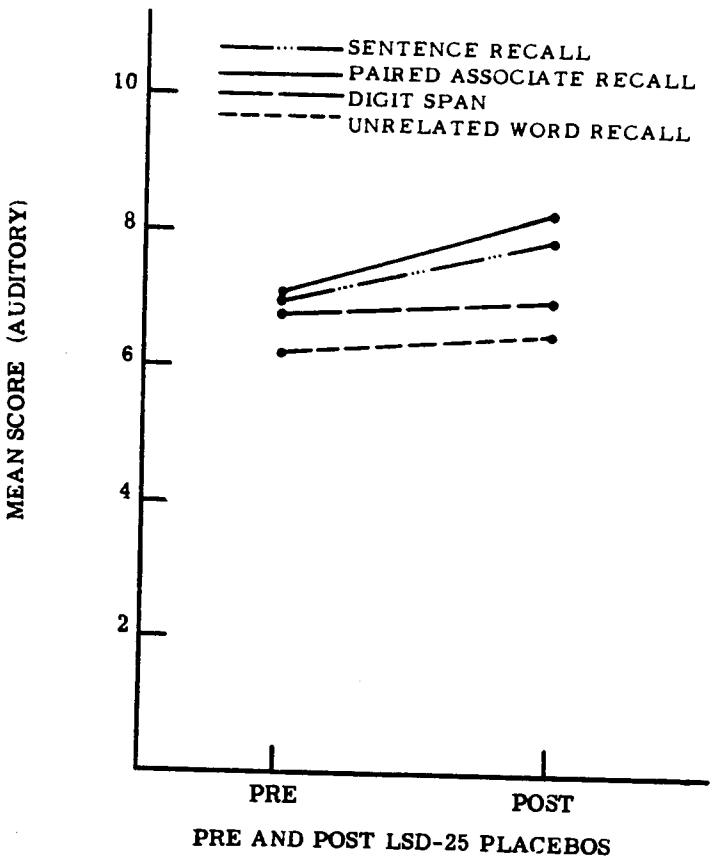

FIGURE 4

Mean number of correct memories on 5 auditory recall and recognition tests. Eight subjects were tested under zero dose LSD-25 before and after drug tests.

apparently occurred even during poor performance. Although only some of the score decrements were significant and only one pre-post improvement was significant, the trend indicates that steady improvement without the drug was to be expected.

The consistent increase of scores on the post-LSD-25 zero dose over the pre-LSD-25 scores might indicate that there is a practice effect which would

be more significant if a larger population were used. This in turn suggests that the decrements in score under the increasing drug doses are more significant than they appear to be. Where improvement was anticipated on a

TABLE 1
PROBABILITY OF CHANCE OCCURRENCE OF SCORE DIFFERENCES BETWEEN DRUG DOSES (N = 12)

	LSD-25 Dosages compared					
	Pre-Drug-Zero vs. 50 Micrograms		Pre-Drug-Zero vs. 100 Micrograms		50 Micrograms vs. 100 Micrograms	
Test	Dir. of change	*P*	Dir. of change	*P*	Dir. of change	*P*
Visual						
letter recognition*	L	—	L	<.02	L	—
nonsense syllable recognition*	L	—	L	—	N	—
object recall	L	.05	L	<.05	L	—
word opposite recall	H	—	L	.05	L	.05
nonsense syllable recall	L	—	L	.02	L	.05
Auditory						
sentence recall	L	—	L	<.01	L	—
paired associate recall	H	—	L	<.05	L	.05
digit span	H	—	H	—	N	—
unrelated word recall**	L	—	L	—	L	—

Notes:
P indicates probability of chance occurrence of difference.
— indicates that *P* is greater than .05.
L signifies lower score under higher dose.
H signifies higher score under higher dose.
N signifies no change in score.
* Score corrected for guessing.
** N = 8.

second and/or third administration of the same tests, impairment frequently appeared. If the form of the learning curve were known, drug scores could be compared with anticipated scores after an equivalent number of repetitions. No norms were available, however, and for practical reasons could not be established in this study.

It was expected that, analogizing from Jost's law (11), tests involving familiar items, numbers, words, and letters would most likely be less affected by LSD-25 than tests using unfamiliar items. Although digit span bears this out, letter recognition, word opposite recall, and sentence recall showed impairment under the drug, while an unfamiliar item, nonsense syllable recognition, showed no significant change under the drug. Recall of nonsense syllables, however, showed very significant impairment under the drug. It is not only the material which must be remembered but the method by which

the memory is tested which must be considered. In another of the studies in this series it was found that on the Wechsler-Bellevue Intelligence Scale the subjects under the drug had significantly lowered "information" scores while their digit span score remained constant.

TABLE 2
SPEARMAN RANK-ORDER CORRELATION OF SUBJECT'S SCORES
(Three LSD-25 doses are correlated, two at a time; N = 12)

Test	LSD-25 Dosages correlated: Pre-Drug-Zero vs. 50 Micrograms		Pre-Drug-Zero vs. 100 Micrograms		50 Micrograms vs. 100 Micrograms	
	ρ	P	ρ	P	ρ	P
Visual						
letter recognition	.14	—	.11	—	.43	—
nonsense syllable recognition	.19	—	.27	—	.77	<.01
object recall	.20	—	.51	—	.06	—
word opposite recall	—.09	—	.28	—	—.01	—
nonsense syllable recall	.26	—	.49	—	.84	<.01
Auditory						
sentence recall	.29	—	.66	<.05	.66	<.05
paired associate recall	.14	—	.74	<.01	—.08	—
digit span	.65	<.05	.52	—	.69	<.05
unrelated word recall*	—.08	—	—.08	—	.74	<.05

Notes:
ρ is the Spearman rank order correlation coefficient.
P indicates the probability that the correlation could occur by chance.
— indicates that P is greater than .05.
* N = 8.

If we consider that adults are always learning number sequences, addresses, telephone numbers, and train schedules, the fact that there was no significant change of digit span under the drug could be taken to mean that the subjects are quite familiar with this learning situation and have a practiced skill in this type of learning that is very difficult to disrupt. With the other "familiar" items the subjects have not usually had such consistent, every-day practice. However, an *a priori,* non-empirical decision as to which items are more difficult, complex, or unfamiliar, may not be feasible.

The findings reported in Table 2 suggest that the scores on tests of memory under one dose tend to be independent of the scores made under another dose. The significant correlations between 50 and 100 microgram score ranks on the nonsense syllable recognition test, and between the score ranks under zero and 50 micrograms, and those under 50 and 100 micrograms on the digit span test indicate reliability of these tests since the average scores were the same or only slightly different for these comparisons.

The significant correlations between the two drug doses on nonsense syllable recall, and between zero and 100 micrograms on sentence recall and paired associate recall do show that on these tests prediction of a subject's position within the group is possible with an acceptable degree of success. Sentence recall and unrelated word recall also showed significant correlations between the two drug doses. However, the score changes were not significant, and the correlations are of little value for predicting. They do indicate that the tests are reliable.

The results show that LSD-25 has a deleterious effect upon the recall and recognition of various kinds of visual and auditory stimuli. They do not indicate whether the impairment is due to the inability to learn, the inability to retain, or the inability to express what has been remembered. Perhaps the impairment results from inadequate attention to the stimuli. Jarvik *et al.* (5) demonstrated that LSD-25 does reduce the ability of a subject to attend and to concentrate.

E. Summary and Conclusions

Twelve non-psychotic adults were tested with nine tests of recognition and recall under a 50 and 100 microgram dose of lysergic acid diethylamide, and under a zero placebo before and after the LSD-25 tests. The following tentative conclusions can be drawn:

1. One hundred mircograms of LSD-25 significantly impaired recognition or recall on six of nine tests, when compared to placebo performance.
2. Fifty micrograms of LSD-25 produced an insignificant effect on recall and recognition.
3. Only sentence recall showed significant improvement from pre- to post-LSD-25 placebo sessions. All tests showed some improvement, however.
4. It is possible to predict a subject's rank position under 100 micrograms from his position under zero micrograms on sentence recall and paired associates recall tests. It is also possible to predict his position under 50 micrograms on nonsense syllable recall. Scores will be different, however, under the two doses.
5. Digit span and nonsense syllable recognition are reliable tests showing no significant changes under the drug.

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Neurology Department
Mount Sinai Hospital
Fifth Avenue and 100th Street
New York City 29