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CERTAIN EFFECTS OF MESCALINE AND LYSERGIC ACID ON PSYCHOLOGICAL FUNCTIONS*

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A. INTRODUCTION

During the past few years the psychiatric use of mescaline and lysergic acid (d-LSD-25) with mental patients as an aid for diagnosis and prognosis and as a potential therapeutic measure has received growing attention. The underlying idea is that these drugs have differential effects among normal subjects and the various categories of psychotic patients. Among psychiatric patients, in many instances, these drugs temporarily and markedly aggravate the mental symptomatology, while in normal persons these agents have the effect of disorganizing mental integration.

The vivid hallucinations following the ingestion or injection of mescaline are well-known phenomena. Less well known is the effect of lysergic acid. The administration of this drug may result in hallucinations of any sense modality. Hoch, Cattell, and Pennes (4, 5, 6) related the hallucinations after ingestion of mescaline or lysergic acid to psychopathological characteristics or basic personality trends of the subject. Klüver (8, 9) stressed the sensory changes brought about by mescaline and emphasized the fact that hallucinations occurred in sensory modalities other than vision. Klüver also pointed out that the hallucinatory mechanisms represent general sensory and perceptual characteristics, so indicating that mescaline is an agent by means of which certain fundamental problems in both biology and psychology might be studied.

Such suggestions represent a challenge to psychologists to scrutinize closely the action of these drugs, to determine which psychological functions are modified by the drugs, and which are left intact. We have found no report of the measurement of psychological functions under experimental conditions following the administration of mescaline and lysergic acid in the literature. Any attempt to make a systematic study of these effects entails difficulties since it is to be expected that the vivid hallucinations brought about by the

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drugs may have a disturbing effect on most varieties of test performance which might be used.

During the spring of 1951, data on sensory and motor performance were collected by Mr. Stanley Fisher, Mr. David Lascowitz and Miss Lillian Siracuse from seven patients at the Psychiatric Institute who were given mescaline and/or lysergic acid by Drs. P. H. Hoch, J. P. Cattell, and H. H. Pennes. We are indebted to both the psychologists and psychiatrists for these data. Opportunity to report this material did not afford itself until the present time.

B. Method

In the selection of a test battery the criterion employed was that the test performance should be sensitive enough to reflect changes which could clearly be attributed to the chemical agents. The functions measured should be of a rather stable nature, and ones not too likely to be disturbed by hallucinations. Test selection was guided by the experience gained during the study of the effect of psychosurgery on psychophysiological functions (1) and from studies made on the effects of chemical agents (2, 10, 11). The Speed and Endurance of Tapping and the Purdue Pegboard were chosen as measures of psychomotor functions, Critical Flicker Fusion as a measure of retinal and/or cortical sensory function, and Pain Threshold as a test of somaesthetic function.

1. *Purdue Pegboard*

The Purdue Pegboard is a finger dexterity test widely used in industry. It provides a measure of the speed of small finger movements with the hands used separately or simultaneously. The subject is required to place small pegs in holes as rapidly as possible with first the right hand, then the left hand, and then using the two simultaneously during successive 30-second periods. The score (Purdue RLB) is the total number of pegs the subject can place during the three periods. He is then required to make assemblies of small parts (pegs, washers, collars) in a designated fashion using both hands as rapidly as possible during a one-minute interval. The score (Purdue Assembly) is the number of pieces assembled during the given interval (Tiffin and Asher, 12).

2. *Tapping Speed; Tapping Endurance*

The procedure and the equipment were the same as that utilized in a previous study by Landis and Zubin (10).

3. *Critical Flicker Fusion Threshold*

The procedure and the Strobotac equipment were the same as that used by Landis and Zubin (10), (CFF-S),. except that three levels of luminance were employed. These were produced by the introduction of Wratten neutral density filters before the test patch which resulted in 7.8, 1.96, and 0.78 millilamberts, test patch luminance.

4. *Pain Threshold*

Pain threshold determinations after the method of Hardy, Wolff, and Goodell (3) were included in the test battery, but the thresholds obtained showed such a marked variation that the data cannot be systematically reported.

C. Subjects

Eleven psychiatric patients (5 male, 6 female; aged 20-54 years; all diagnosed as schizophrenia; and all in the early stages of the disease) constituted the group studied.

Four of the patients served as a control group. and the remaining seven constituted the experimental group. Five patients in the experimental group were given synthetic mescaline sulphate intravenously. One patient received 0.35 gram of the drug while the others received 0.50 gram. Complete data were obtained on all five patients for the Tapping and Purdue Pegboard tests during the period of mescaline intoxication. One patient (No. 5) was unable to do the CFF tests after receiving mescaline. Patients Nos. 2, 3, and 5 experienced hallucinations while Nos. 1 and 4 did not.

Four of the patients included in the mescaline group, and an additional two patients, on whom it had not been possible to obtain data during mescaline, were tested following the ingestion of lysergic acid. One patient (No. 4) was given 0.10 mg of lysergic acid; one (No. 6) was given 0.06 mg first, followed by 0.12 mg 1½ hours later; while the remaining four were given 0.12 mg. In all instances the lysergic acid was given orally. Three (Nos. 2, 3, and 6) of the six patients experienced hallucinations following ingestion of lysergic acid. All three had visual hallucinations; in addition two of the three had auditory and one of the three had olfactory hallucinations.

The patients were given all tests on two or three successive days before mescaline or lysergic acid was administered. Since the number of these test days varied, we have used the last test prior to drug administration as our "pretest" base. The patients were tested about 1½ hours after the drug had been administered, which will be referred to as the "Drug" test. They were

again tested about 6 hours after the drug administration which will be referred to as "Post 1" test. Finally they were tested during the morning of the day following the drug treatment, which will be referred to as "Post 2" test. The lysergic acid was administered several days after the mescaline so that the "Post 2" test of the mescaline experiment served as "Pretest" for the lysergic acid experiment for those patients who received both drugs. The patients were tested about 1½ hours after ingestion of lysergic acid ("Drug"), 6 hours after ingestion ("Post 1"), and during the morning of the following day ("Post 2").

The patients in the control group were subjected to the same test battery and to the same test schedule as far as Pretests were concerned. The "Drug," "Post 1," and "Post 2" sessions were one day apart. (The terms "Drug," "Post 1," and "Post 2" sessions, as applied to the control group, really refer to the first, second, and third sessions following the Pretest baseline, since no drug was employed.)

D. Results

The group averages, standard deviations, and per cent of change based on the pretest level for the various test performances, are given in Table 1. It will be noted that the Pretest score level (except for the Purdue Assembly) of the control group was slightly superior to that of the mescaline or lysergic acid group. Since all three groups were small, the usual tests for statistical significance have not been applied. Our evaluaton of any change in test performance must rest on the size and consistency of the changes as well as on our knowledge of possible experimental errors. Figure 1 gives in a comparative fashion a graphic presentation of the per cent change in score from the pretest score taken as 100 per cent for each test at each test period for the mescaline, lysergic acid, and the control group.

From both Table 1 and Figure 1, it is evident that the mescaline dropped all mean scores for the Purdue Pegboard and Tapping well below those made by the control patients at the equivalent test periods. The loss in efficiency is most marked 1½ hours after injection ("Drug"); it is still evident 6 hours after injection (Post 1), while 24 hours after injection (Post 2) the efficiency is still below that of the control group.

The effect of mescaline on CFF (if any) is unclear with the possible drop of 10 per cent 1½ hours after, and gain of 10 per cent 6 hours after mescaline injection, at the lowest level of luminance. If these changes were significant they probably indicate that mescaline affected only the low intensity CFF thresholds.

TABLE 1

MEANS (M), STANDARD DEVIATIONS (σ) AND PER CENT OF CHANGE (%) AT EACH TEST PERIOD FOR THE MESCALINE, LYSERGIC ACID, AND CONTROL GROUPS

Test	Group	N	Pretest			Drug			Post 1			Post 2		
			M	σ	%	M	σ	%	M	σ	%	M	σ	%
Purdue RLB	Mescaline	5	41.6	8.6	100	37.2	4.9	89	38.0	8.2	91	42.2	9.1	101
	Lysergic	6	41.7	8.0	100	38.3	6.9	92	38.8	5.2	93	42.5	6.4	102
	Control	4	43.5	5.1	100	44.0	4.9	101	44.3	6.6	102	44.8	5.4	103
Purdue Assembly	Mescaline	5	34.4	5.2	100	26.0	8.1	76	28.0	9.1	81	32.4	8.5	94
	Lyseric	6	30.7	8.0	100	31.7	9.1	103	29.3	8.3	95	34.3	8.4	112
	Control	4	31.5	8.6	100	35.5	5.1	113	38.0	7.0	121	40.0	5.0	127
Tapping Speed	Mescaline	5	106.0	36.4	100	95.4	35.7	90	102.4	37.0	97	110.6	36.1	104
	Lysergic	6	110.8	31.5	100	123.2	29.9	111	112.7	19.3	102	115.5	25.3	104
	Control	4	125.8	34.7	100	125.0	28.4	99	125.0	22.2	99	134.0	29.5	106
Tapping Endurance	Mescaline	5	221.8	68.8	100	211.2	74.5	95	205.6	70.9	93	221.2	73.1	98
	Lysergic	6	228.5	49.3	100	234.5	43.6	103	214.5	30.4	94	245.0	53.9	107
	Control	4	249.3	47.7	100	256.8	43.3	103	259.5	32.7	104	267.3	35.6	107
CFF 0.78 ml	Mescaline	4	34.5	4.8	100	31.0	7.1	90	37.8	6.4	110	35.2	3.4	102
	Lysergic	6	35.5	4.3	100	34.8	4.7	98	35.7	5.4	101	36.1	3.6	102
	Control	4	37.0	2.9	100	35.6	5.7	96	37.5	4.6	101	35.4	1.5	96
CFF 1.96 ml	Mescaline	4	36.6	3.2	100	37.7	6.4	103	39.7	5.5	108	37.9	4.7	103
	Lysergic	6	38.1	4.4	100	36.6	4.2	96	38.0	4.1	100	37.5	3.7	98
	Control	4	39.0	4.5	100	35.9	5.6	92	36.5	1.9	94	37.0	4.2	95
CFF 7.8 ml	Mescaline	4	41.8	2.8	100	43.7	3.9	104	42.6	3.5	102	42.9	4.5	103
	Lysergic	6	40.8	4.6	100	40.9	4.3	100	42.2	3.0	103	42.6	3.5	104
	Control	4	42.8	4.7	100	45.4	4.1	106	43.0	3.0	101	42.8	3.5	100

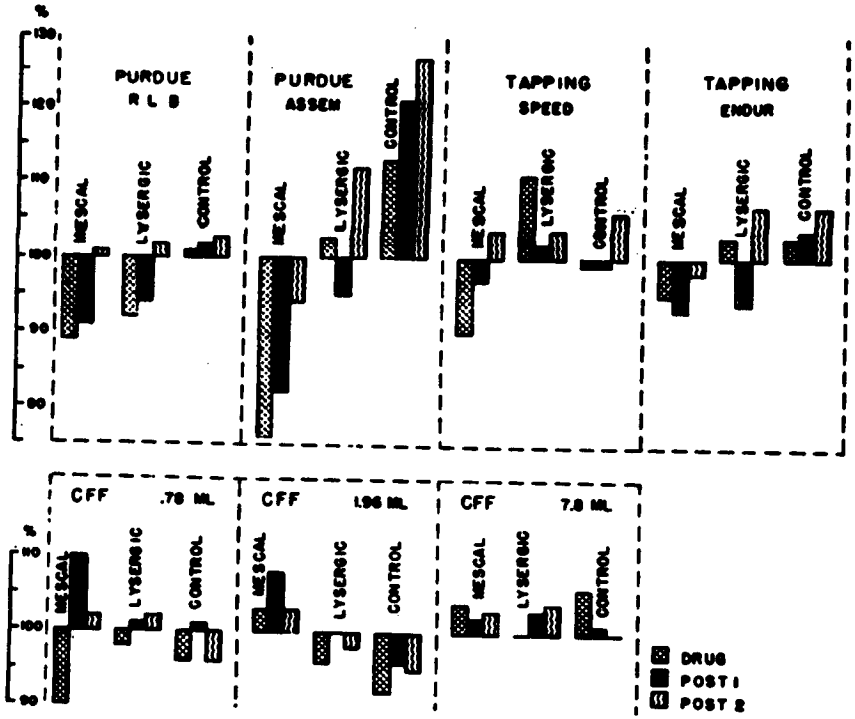

FIGURE 1

TEST SCORES AT EACH TEST PERIOD AS PER CENT OF THE PRE-TEST LEVEL FOR THE MESCALINE, LYSERGIC ACID, AND CONTROL GROUPS

From Table 1 and Figure 1, it will be seen that lysergic acid increased the mean score for Tapping Speed by 11 per cent 1½ hours after ingestion of lysergic acid (Drug) with a return to pretest level 6 hours after ingestion (Post 1). Smaller mean changes of doubtful significance appear in the Tapping Endurance and Purdue Assembly scores. The Purdue RLB score shows a loss of 8 per cent at 1½ hours, 7 per cent at 6 hours, with a return to pretest level at 24 hours. The changes in CFF are minor and probably do not exceed the experimental variability.

It was not to be expected that all patients would react in the same way and to the same degree to the mescaline or to lysergic acid. In Table 2 are given the directions of change (increased or decreased score efficiency) at 1½ hours after injection of mescaline (Drug) and at both 1½ and 6 hours after ingestion of lysergic acid (Drug and Post 1) in contrast to the pretest

TABLE 2

CHANGES IN DIRECTION OF SCORE 1½ HOURS AFTER RECEIVING MESCALINE AND 1½ AND 6 HOURS AFTER INGESTION OF LYSERGIC ACID

Patient Number	Dosage	Hallucinations	Purdue RLB	Purdue Assembly	Tapping Speed	Tapping Endurance	CFF— .78 ml	CFF—1.96 ml	CFF—7.8 ml
Mescaline—1½ hours									
1	.50 gr	—	—	—	—	+	+	—	—
2	.50 gr	+	—	—	—	—	—	+	+
3	.35 gr	+	—	—	—	+	—	+	+
4	.50 gr	—	—	—	+	—	—	+	+
5	.50 gr	+	0	—	—	—	x	x	x
Lysergic Acid—1½ hours									
1	.12 mg	+	—	0	+	+	+	—	—
2	.12 mg	+	—	+	+	—	+	—	+
3	.12 mg	+	0	+	0	+	—	—	—
4	.10 mg	—	—	0	+	—	+	—	+
6	.06 mg	+	—	—	+	+	—	—	+
7	.12 mg	—	—	+	+	+	—	—	—
Lysergic Acid—6 hours									
1	.12 mg	?	+	+	—	—	+	+	+
2	.12 mg	+	—	—	—	—	—	+	+
3	.12 mg	+	+	—	+	—	+	—	+
4	.10 mg	—	0	—	—	—	+	+	—
6	.18 mg	+	—	—	—	—	+	+	+
7	.12 mg	—	+	0	—	—	+	+	+
No Hallucinations									
1	Mescaline (.50 gr)	—	—	—	—	+	+	—	—
4	Mescaline (.50 gr)	—	—	—	+	—	—	+	+
4	Lysergic Acid (.10 mg)	—	0	—	—	—	+	+	+
7	Lysergic Acid (.12 mg)	—	+	0	—	—	+	+	+
Hallucinations									
2	Mescaline (.50 gr)	+	—	—	—	—	—	+	+
2	Lysergic Acid (.12 mg)	+	—	—	—	—	—	+	+
3	Mescaline (.35 gr)	+	—	—	—	+	—	+	+
3	Lysergic Acid (.12 mg)	+	+	—	+	—	+	—	+
5	Mescaline (.50 gr)	+	0	—	—	—	x	x	x
6	Lysergic Acid (.06 mg)	+	—	—	—	—	+	+	+

scores. Since lysergic acid was given by mouth and since Table 1 showed that there was still some evidence of changed scores at Post 1, we have made the additional entries for lysergic acid changes at 6 hours after ingestion.

Inspection of Table 2 shows several interesting points. No patient had an increased Purdue RLB score 1½ hours after either drug, while all patients had a lowered score on Purdue Assembly following mescaline. Lysergic acid gave mixed individual results at 1½ hours and 5 out of 6 scores decreased at

the end of six hours. Mescaline usually reduced both Tapping Scores at 1½ hours while lysergic acid usually was followed by an increased score at 1½ hours and a decrease at 6 hours. The CFF changes at 1½ hours are, with the exception of CFF 1.96 ml following lysergic acid, of mixed direction. (The uniform drop at 1.96 ml with lysergic acid at 1½ hours is not convincing in that the amount of drop was in each case small and well within the range of variation shown by the control patients.) However, after six hours almost all CFF scores are increased. We mentioned earlier that the measurements made of pain threshold were so variable that they could not be reported. The CFF measures are also variable and not very conclusive. Hence neither measure of sensory thresholds gave really satisfactory data. On the basis of more recent and as yet incomplete studies, we are inclined to attribute this difficulty in obtaining sensory thresholds to faulty methodology employed in the collection of these data rather than to variability per se.

The effect of these drugs on motor performance may be summarized in the following fashion:

The Purdue Pegboard scores indicate that both mescaline and lysergic acid decrease the efficiency and/or speed of this rather complicated, coördinated motor response. The mescaline acts more profoundly and rapidly and may persist in effect for as much as 24 hours.

Mescaline interferes with both speed and endurance of simple tapping, the effects continuing as long as 6 hours. With the exception of Purdue RLB, lysergic acid tends to act as an immediate stimulant (1½-hour test) with a decrement in most motor scores in most individuals after 6 hours. The effect of either agent is still evident on tapping scores after 24 hours.

In Table 2 we have noted whether or not the drug produced hallucinations. It will be seen that mescaline at the dosage given produced hallucinations in patients Nos. 2, 3, and 5 while lysergic acid did so in patients Nos. 2, 3, and 6. From the inspection of Table 2 in which we commented about lysergic acid, it seems to show a depressant effect on motor test scores and an increased CFF score 6 hours after ingestion. The last two sections of Table 2 are regrouped on the basis of whether or not hallucinations occurred using the mescaline 1½-hour entries and lysergic acid 6-hour entries. This regrouping provides a clearer picture. All patients who had hallucinations (except No. 3) show decreased motor test scores ("0" entries are properly decreases since some increase with learning would be expected to take place). On the CFF measures all patients (except No. 3) who had hallucinations showed an increased score on the 1.96 and 7.8 ml levels. Patient No. 3

had hallucinations following both mescaline and lysergic acid but did not follow completely the pattern of performance of the other hallucinated patients.

The pain threshold determinations were extremely variable, both with regard to any one subject and between the various patients. We were not able to detect any systematic trend in the data. Particularly confusing was the fact that some of the obtained thresholds were completely out of the standard range of variability. We are inclined to attribute this excessive variability of threshold following the two drugs to inherent difficulties in the particular technique, rather than to any real unusual variability of threshold.

E. Discussion

These experiments demonstrate that controlled objective psychological experiments can be performed when an observer is under the influence of mescaline or of lysergic acid. In other words, neither the "disintegration of personality," the various hallucinations, the existing psychopathology, nor any combination of these, make it uniformly impossible for these patients to coöperate and to provide reasonably stable measures on certain specific tests.

The effect of the injected mescaline was shown by the tests employed 1½ hours after the injection and was still apparent 24 hours after injection so far as the tapping test scores were concerned. When the mescaline produced hallucinations the test scores were, in general, changed more markedly. In the case of patient No. 5, the visual hallucinations were so pronounced that he could not provide satisfactory CFF thresholds although he could do the motor tasks.

The ingestion of lysergic acid, in general, started hallucinations within 1½ hours after taking, and during this initial period tended to produce some increase in the motor test scores. By 6 hours after ingestion, almost all motor test scores were reduced especially if the patient had experienced hallucinations. The CFF threshold was usually increased for the highest brightness level.

That different individuals are affected differentially by different drugs, and that different dosage levels of drugs produce different effects is well known. Considering these points, as well as the limited number of patients involved in this study, the general consistency of results is rather remarkable.

F. Summary

Patients in the early stage of schizophrenia were used as subjects in a tapping test, in the determination of the critical flicker-fusion threshold and in the Purdue Pegboard test. Five of these patients received synthetic mesca-

line sulphate intravenously, six ingested lysergic acid (d-LSD-25), and four served as a control. The tests were repeated several days prior to the administration of the drug, and 1½ hours, 6 hours, and 24 hours following the administration.

1. In spite of the marked effect of mescaline and lysergic acid on sensation, perception, and general symptomatology of the mental patient, it was possible to measure quantitatively the changes in efficiency reflected by the objective test scores.

2. If the drug induced hallucinatory experience, the changes in test scores tended to be more consistent.

3. Injection of mescaline resulted in a marked mean drop for the group in Tapping and Purdue Pegboard scores 1½ hours following injection which decrease was still apparent 24 hours after injection in the Purdue Assembly and Tapping Endurance scores.

4. Ingestion of lysergic acid (d-LSD-25) produced visual hallucinations in three of six patients. The group mean Purdue RLB score was decreased and the other three motor test scores somewhat increased 1½ hours after ingestion. Six hours after ingestion, except for tapping speed, all group means for the psychomotor tests were reduced, and the scores for the two higher levels of brightness at which CFF was determined were somewhat increased.

5. Analysis of the change in direction of test score performance for each individual concerned showed that when the patient was hallucinated by the drug the individual test results were fairly uniform. Mescaline generally resulted in decreased motor test and lower CFF scores 1½ hours after injection. Lysergic acid usually produced decreased motor test scores and increased CFF thresholds for the highest level of luminance six hours after ingestion.

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