(107)

COMPARISON OF THE EFFECTS OF MLD-41 AND LSD-25

MLD-41 is l-methyl-diethylamide of lysergic acid. Studies on this agent were undertaken in order to obtain data on structure-activity relationships in the LSD series.

The purposes of the present experiments were: (1) to determine if MLD induced LSD-like effects; and (2) to assess roughly the potency of MLD as compared with LSD.

METHODS

Subjects. Fourteen Negro males aged 24 to 45 years volunteered for the experiments. All were prisoners who were serving sentences for violation of the U. S. narcotic laws and all had been abstinent from narcotic drugs for at least six months prior to serving in these experiments. All were in good physical and mental health, none were psychotic, and all had taken LSD on previous occasions.

Drugs. The drugs were given orally in solution. Identities of the drugs were unknown to both the patients and observers. Observers did not know of the purposes of the experiments, and, furthermore, were not aware that a new LSD-like drug was being

A-366

given. Solutions of the drugs were prepared with freshly distilled water and preserved in brown bottles; concentration of stock solutions was 100 mcgm./cc. Doses for each individual were measured with micro-pipettes and drugs diluted to 30 cc. with freshly distilled water and administered while patients were fasting.

Methods of Measurement. Patients were housed in a special ward which is reserved for experimentation with psychotomimetic drugs. The patients entered this ward on the night before tests. All were accustomed to the environment. At hourly intervals, two hours before and eight hours after administration of drugs, the pupillary diameter was measured under conditions of controlled light and accommodation. The distance through which a calibrated hammer must fall to elicit a kneejerk was determined. Systolic blood pressure was measured after ten minutes rest in bed. Patients filled out a modification of the Abramson-Jarvik questionnaire hourly, and short mental-status examinations were made by the attending physician. Data on pupillary size, blood pressure, and threshold for elicitation of kneejerk were plotted on graph paper and the average of the two pre-drug observations used as a baseline. Data under the curve for the 8-hour period of observation was measured with a planimeter, thus reducing all data on these particular measurements to a single figure. Questions were counted, eliminating any that were also

A-365

scored positively prior to ingestion of the drug. Clinical grade was assessed according to the method of Isbell, as described in the attached reprint.

Dosage. Patients received, in randomized order: placebo; LSD 1 mcgm./kg. (10 subjects); LSD 1.5 mcgm./kg. (10 subjects); and LSD 2 mcgm./kg. (8 subjects); and various doses of MLD-41. In order to ascertain the approximate dosage range, preliminary runs were done with MLD-41. With doses of .25 mcgm./kg. (1 patient), 0.5 mcgm./kg. (1 patient), 0.75 mcgm./kg. (1 patient), or 1 mcgm./kg. (1 patient), no objective or subjective effects were observed. However, when 1.5 mcgm./kg. (3 patients) or 2 mcgm./kg. (1 patient) were given, definite, but mild, LSD-like mental symptoms were observed. It was, therefore, decided that experimental doses would be higher than 2 mcgm. of MLD-41 per kg. Six patients received 3 mcgm./kg. of MLD-41, 10 received 4 mcgm./kg., and 6 received 6 mcgm./kg.

RESULTS

Results are shown in the table. In reading the table, figures represent the mean for the particular measurement ± the standard error. The data, however, are sufficient to show that: (1) MLD creates autonomic disturbances similar to those caused by LSD; (2) MLD creates psychic disturbances similar to those caused by LSD; (3) MLD is less potent than LSD. The data permit a rough estimate that LSD is one-third to one-half as potent as

A-364

LSD. Such a figure is only an approximation since true dose-response curves cannot be constructed because number of patients at each dose was too small, some patients did not receive all doses, and, apparently, flat portion of the dose-response curve had already been reached with the 4-mcgm./kg. dose in case of kneejerks, pupillary size, and blood pressure.

Subjective phenomena reported after ingestion of MLD-41 included anxiety, feelings of unreality, confusion, haptic sensations, alterations in tactile, visual, and auditory perception, the presence of delusions and optic hallucinations, depersonalization and derealization. The MLD-reaction began more slowly (usually 1 to 1-1/2 hours as compared to 30 minutes after LSD) and did not persist as long.

CONCLUSIONS

MLD-41 is a psychotomimetic drug which induces mental effects similar to those of LSD. It is roughly one-third to one-half as potent as LSD.

A-362

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ISUES	DRUG AND DOSE						
		LSD Mcgm./Kg.			MLD Mcgm./Kg.		
	Placebo	1.0	1.5	2.0	3.0	4.0	6.0
ejerk	0.38 ± 0.2	2.40 ± 0.34	2.60 ± 0.36	2.39 ± 0.54	3.04 ± 0.35	3.10 ± 0.28	2.86 ± 0.49
illary e	0.94 ± 0.4	4.42 ± 0.34	4.53 ± 0.52	4.82 ± 0.47	4.55 ± 0.66	4.96 ± 0.47	4.61 ± 0.5
od ssure	0.89 ± 0.16	2.46 ± 0.36	2.50 ± 0.04	2.63 ± 0.39	2.83 ± 0.37	2.87 ± 0.41	3.18 ± 0.5
tions	1.0 ± 3.3	36 ± 13	55 ± 22	48 ± 15	19 ± 22	34 ± 19	42 ± 13
al ds	0 ± 0	1.0 ± 0.35	1.5 ± 0.4	1.8 ± 0.37	1.0 ± 0.55	1.3 ± 0.3	2.0 ± 0.32

Number of subjects at various doses: LSD 1.0 mcgm./kg. (10 subjects); LSD 1.5 mcgm./kg. (10 subjects); LSD 2.0 mcgm./kg. (8 subjects); MLD 3.0 mcgm./kg. (6 subjects); MLD 4.0 mcgm./kg. (10 subjects); MLD 6.0 mcgm./kg. (6 subjects).

Figures are means ± standard errors.