

Methylenedioxyamphetamine (MDA)

Subjective Effects

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The modern history of investigations into the psychotherapeutic potential of drugs displaying psychotropic effects probably begins with the studies of hashish carried out over a century ago.³ Over the intervening decades many compounds have been examined for this purpose with increasing scientific acumen.¹² In more recent times, LSD has been the focus of considerable interest in this regard,²⁰ especially since a growing awareness of the significance of set and setting in influencing various parameters of drug action made it possible to exercise a greater degree of control in directing the course of a drug experience toward therapeutic objectives.^{20,21} In our own facility, a continuing series of experimental studies of LSD assisted psychotherapy in the treatment of alcoholics,⁷ neurotics,¹⁰ the psychological care of the cancer patient,¹⁴ and narcotic addicts¹⁶ have been pursued with encouraging findings. Most recently, our attention has turned to other compounds that might be more readily utilized than LSD. In this pursuit, studies were carried out with Dipropyltryptamine (DPT), a compound with hallucinogenic properties somewhat similar to LSD but of considerably shorter duration of action.^{5,19}

In 1959, Alles reported on his studies of analogues of mescaline¹ and specifically on Methylenedioxy-

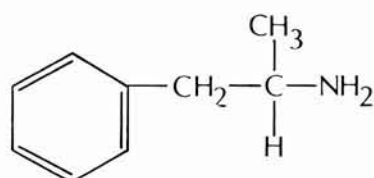
amphetamine (MDA). Several of these phenylisopropylamine compounds, frequently but incorrectly referred to as "amphetamines," have in recent years been the object of study, among them 2,5 dimethoxy-4-methylamphetamine (DOM) and 2,5 dimethoxy-4-ethylamphetamine (DOET)^{2,4,18} (see Figure 1). Alles selected MDA for a series of self-experiments¹ and reported that the compound, though it was not hallucinogenic, did heighten perception, citing that he could hear sounds that were usually inaudible. Alles reported that the threshold dose for the appearance of subjective effects was about 80 mg. He noted as side effects some increase in blood pressure and pupillary dilation and stated that the effects of MDA in preventing sleep were substantially less than amphetamine. Naranjo and his associates, in 1967, tested MDA as a possible adjunct to psychotherapy.^{11,17} Utilizing volunteers who had previously experienced the effects of other psychoactive agents such as LSD, they confirmed that MDA was not hallucinogenic but that other effects, similar to those produced by LSD, could be obtained. In a dosage from 40 to 150 mg., none of the subjects reported hallucinations, perceptual changes, impaired thinking or eyes closed imagery. Yet, the subjects reported that, at some point during the drug action, MDA brought about an intensification of feeling, a facilitation of insight, and heightened empathy. It was also reported that the psychotropic effects of this compound reached a peak intensity within two hours, with some effects continuing for approximately eight hours. It was these rather promising observations that led to the initiation of the present study.

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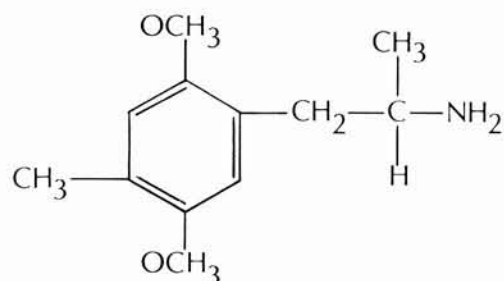
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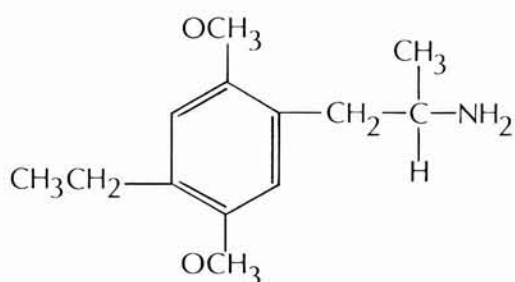
FIGURE 1 :



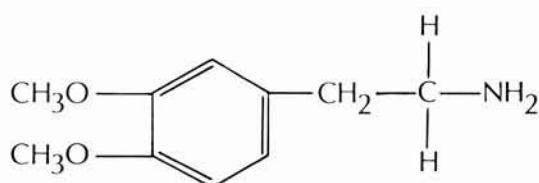
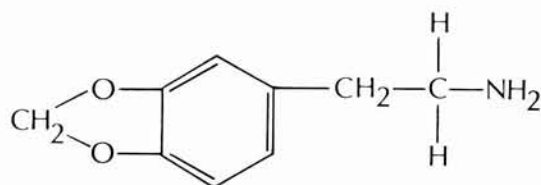
Amphetamine



2,5, dimethoxy-4-methylamphetamine (DOM)



2,5, dimethoxy-4-ethylamphetamine (DOET)

3,4,5-trimethoxy-B-phenylethylamine
(Mescaline)2-amino-1-(3,4-methylene-
dioxyphenyl)-propane

Methylenedioxyamphetamine (MDA)

METHOD

Ten subjects were selected to investigate the subjective effects of MDA. These were volunteers from the professional staff of the Maryland Psychiatric Research Center, nine of whom had previously experienced the effects of LSD under the carefully controlled experimental conditions in the Research Center.

Each subject ingested the levo-isomer of MDA in a fixed oral dose of 75 mg. at 9:00 A.M., in the same experimental setting in which the LSD and DPT studies were being conducted: a comfortably furnished room which could be monitored through a closed-circuit video system. Throughout the period of drug action, a staff psychotherapist and a nurse were in constant attendance. Each subject remained within the unit for the entire period of the drug experience, and except for short periods of psychometric and physiological testing, repeated every 60-90 minutes, the subjects spent their time either conversing with the therapist and nurse or reclining and listening to music with stereophonic headphones and eye shades.

Blood pressure and respiration were recorded prior to the ingestion of the drug and every hour thereafter up to the seventh hour.

The Digit Span and Digit Symbol Subtest of the Wechsler Adult Intelligence Scale were administered before taking the drug and every 90 minutes up to the eighth hour. The Digit Span Subtest was employed as a measure of immediate memory and ability to concentrate. The Digit Symbol Subtest was utilized as a measurement of the subject's ability to rapidly perform visual motor tasks.

Handwriting was examined as a possible indicator of emotional expansiveness by comparing a four line handwriting sample of a nursery rhyme verse obtained prior to the drug experience and subsequently obtained at several points at the same time throughout the drug experience. It was hypothesized that the greater the amount of space utilized, the greater would be the degree of emotional expansiveness experienced by the subject.

Three questionnaires were utilized to assess the subjective effects of the drug experience: the Psychedelic Experience Questionnaire;¹³ the Subjective Drug Effects Questionnaire;⁶ and the Ludwig-Levine Modification of the Linton-Langs Questionnaire.⁸

1) The Psychedelic Experience Questionnaire had originally been constructed to study the nature of the mystical experience occurring either spontaneously or induced by psychedelic compounds.¹³ This questionnaire, revised by Pahnke and Richards, was the one

employed in the present study (see Appendix 1). In its present form, it includes 100 items. These are rated by the patient or subject after the drug experience with each item rated on a scale of intensity from 0-6. These are summed up by ratings of certain precoded items to derive scores for such so-called "mystical" factors such as unity, transcendence of time and space, sacredness, deeply felt positive mood, ineffability, and paradoxicality.

2) The Linton-Langs Questionnaire was originally designed by Linton-Langs⁸ as a tool to assess the general subjective reactions to LSD. The current modification was produced by Ludwig-Levine⁹ for use in their study of the treatment of alcoholics with LSD. The current version of the scale consists of 89 items which have been grouped on an a priori basis into eight scales: 1) alteration of thinking, 2) disturbed time sense, 3) loss of control, 4) meaning change, 5) affect change, 6) body image change, 7) somatic change, and 8) perceptual change.

3) The Subjective Drug Effects Questionnaire⁶ consists of 272 questions designed to survey the drug effects. In utilizing this questionnaire in the present study, four major scales were scored to determine drug effects upon: Thinking (20 items), Feeling (54 items), Perception (43 items), and Somatic Changes (53 items).

RESULTS

A. Physiological Responses

1) *Blood pressure, pulse and respiration.*—There was a nonsignificant drop in systolic blood pressure at the first hour, followed by a significant rise at the second hour ($p < .01$), third hour ($p < .05$), and a return to pre-drug levels at the fifth hour. The highest average increase was 11.0 mm. at the second hour. One subject, a 52-year old woman, had a 40 mm. increase at the third hour. Diastolic blood pressure did not fluctuate significantly through out the period of drug action. There was a slight but nonsignificant increase in pulse rate in the second through fourth hours. The highest average increase was eight beats per minute at the third hour. Respiration rate did not change significantly.

B. Psychometric Assessments

1) *Digit Symbol Subtest.*—There was a slight but significant decrement in performance starting at the first hour after drug ingestion, which continued until returning to the pre-drug level at the sixth hour. The greatest decline was shown at the third hour when subjects averaged 51.8 completed symbols as compared to their pre-drug level of 59.8 completed symbols.

2) *Digit Span Subtest.*—Subjects reported that they

felt that they were exerting more conscious effort than usual to succeed in this task. Nevertheless, analysis of the Digit Span scores showed no significant changes from baseline evaluation in repeating digits backward and forward throughout the six hours.

3) *Handwriting Test.*—The average amount of space used to write a defined four line verse increased significantly from the pre-drug baseline at one and one half ($p < .05$), three ($p < .05$), four and one half ($p < .01$), and six hours ($p < .01$).

C. Psychedelic Questionnaires

1) *Psychedelic Experience Questionnaire.*—To provide a basis for evaluating the MDA results, the MDA scores were compared with a sample of ten mental health professionals who had had an LSD session in the setting of the Maryland Psychiatric Research Center; the LSD sample having been drawn at random from a larger group of subjects (professionals). Table 2 compares the means and percentages of items endorsed by the LSD and MDA groups.

The trends outlined in Table 2 would indicate that LSD is more likely than MDA to produce unitive experiences involving a sense of ego loss and to provide access to dimensions of awareness that are beyond the usual conceptions of time and space. The LSD experience is also more difficult to describe in logical, rational terms.

MDA-produced changes experienced by the majority of subjects were reflected in the following items of the questionnaire: feelings of peace and tranquility, feelings of tenderness and gentleness, increase in the beauty and significance of music, feelings of emotional closeness with the companion, increased awareness of the importance of interpersonal relationships, feelings of joy, experience of oneness in relation to an inner world within, sense of being at a spiritual height, experience of pure being and pure awareness, gain of insightful knowledge experienced at an intuitive level, feeling that the state of consciousness experienced during part of the session was more real than normal awareness of every day reality, and loss of the usual sense of time.

Items that were least frequently experienced were: feelings of anger or aggression, feelings of despair, experience of confusion, disorientation, feelings of being plotted against, experience of isolation or loneliness, feelings of being rejected or unwanted, experience of life being meaningless and absurd, frustrating attempt to control the experience, feelings of antagonism toward the therapist, sense of being separated from the normal world, fears of losing one's mind or going insane and visions of religious personages.

TABLE 1
BLOOD PRESSURE* AND PULSE OF MDA SUBJECTS**

Subject	Sex	Age	Wht.	Pre- Drug	+1 hr.	+2 hr.	+3 hr.	+4 hr.	+5 hr.	+6 hr.	+7 hr
1	M	41	160	120/80 60	117/80 52	143/80 60	140/80 52	140/80 52	135/80 56		
2	M	48	180	148/98 68	130/70 80	160/100 80	148/90 80	140/90 80	130/90 80	160/90 80	
3	M	33	155	128/88 88	132/96 80	142/106 96	142/108 112	142/106 108	132/98 96	128/86 92	122/84 88
4	M	28	164	130/80 80	128/70 70	140/80 78	130/70 80	138/70 80	120/70 80	130/70 80	130/70 80
5	F	58	160	132/82 72	138/82 78	138/82 70	142/82 82	140/82 88	140/82 78	138/82 80	132/82 72
6	M	42	172	145/70 72	138/80 70	145/60 80	160/90 80	140/80 70	145/70 78	145/70 72	130/80 70
7	M	23	150	122/82 92	120/80 92	132/90 82	148/84 84	146/86 78	140/82 72	142/84 80	130/84 102
8	M	28	165	130/80 65	120/80 65	140/90 70	120/80 70	130/84 84	128/80 72	128/88 80	120/80 80
9	F	52	150	128/78 80	128/76 80	162/112 104	168/108 124	156/94 108	148/86 96	142/82 88	138/78 84
10	M	41	160	128/68 86	128/68 80	128/78 76	128/78 66	122/72 64	122/68 72	120/72 72	120/72 66

* First horizontal line: blood pressure
 ** Second horizontal line: pulse

TABLE 2
SCORES ON THE PSYCHEDELIC EXPERIENCE QUESTIONNAIRE
FOR MDA AND LSD GROUPS

Scale	MDA (N=10)			LSD (N=10)		
	M	S.D.	% of Total	M	S.D.	% of Total
Unity	16.4	8.34	54	20.4	4.80	68
Sacredness	20.2	10.50	57	19.2	9.44	54
Objectivity & Reality	11.4	6.50	57	14.4	4.39	72
Transcendence Time & Space	18.4	11.12	46	28.7	3.72	71
Positive Mood	21.2	9.83	60	21.0	7.66	60
Ineffability	15.7	7.32	62	19.8	2.52	79

2) *Linton-Langs Questionnaire as modified by Ludwig-Levine*.—Table 3 lists the means and percentages of items endorsed on the categories of the Questionnaire. The major effects of MDA are in the area of seeing new or changed meaning in experience (Meaning Change 45%). The drug produces only minimal changes in the sense of body awareness (Body Image Change 14%), while alterations in perception of the external environment are practically non-existent (Perceptual Change 5%). There is a moderate alteration in the perception of time (Disturbed Time Sense 29%). The low score on the Loss of Control Scale (14%) indicates that drug action at this dose level is not experienced as overwhelming or

the subjects, while half indicated that they felt numb, "tingly," and physically weak at some point in the experience.

3) *Subjective Drug Effects Questionnaire*.—Nine of the ten subjects (the same nine who had had LSD) reported that they felt more relaxed, happier and more at peace with the world during the experience. Eight subjects indicated that they felt more calm, more free, more loving and felt more like paying close attention to their surroundings. Six of the subjects reported dryness of the mouth, a loss of appetite, unsteadiness of gait and difficulties in concentrating on external tasks at some time during the drug experience.

TABLE 3
MDA PRODUCED CHANGES AS MEASURED BY
THE MODIFIED LINTON-LANGS QUESTIONNAIRE

Scales*	No. of Items in Scale	M	S.D.	% of Total
Meaning Change	11	4.90	3.14	45
Somatic Change	11	3.55	2.57	32
Disturbed Time Sense	5	1.45	1.23	29
Affect Change	6	1.50	1.20	25
Alteration in Thinking	13	1.95	1.59	15
Loss of Control	15	1.90	2.21	14
Body Image Change	12	1.65	1.30	14
Perceptual Change	16	0.85	0.90	5
*Scales are arranged in the sequence of the scale with the maximum score to that with the least.				

unmanageable.

Identifying the specific items most frequently endorsed, seven of the subjects responded to the item "Sense of being at a spiritual height," while five felt a sense of "oneness with the world or universe." At least half of the subjects reported that as a result of the experience, the meaning of life was clearer, that life has new significance and that they were able to discern new connections between certain events or experiences that they had not been aware of before. Seven of the subjects felt especially joyous and serene during the experience. Over half said that they occasionally lost their sense of time, that thoughts and the sense of time seemed to be moving faster than usual and that they had difficulty concentrating on external tasks. Physical changes consisting of chills or cold feelings were reported by eight of

The percentages of total items endorsed on the four major scales of the test arranged in the sequence from the maximum to minimum score were: Feeling 40%, Thinking 36%, Somatic 24%, and Perception 14%.

GENERAL FINDINGS

The average time of onset of a reaction to the drug was one hour. The range for noticing effects was 30 minutes to 85 minutes. Where a peak intensity was noted this usually was reached within the first two hours. Most subjects reported that they could still feel some effects after 12 hours. During the latter stages that state of mind sometimes became somewhat overactive

and overstimulated, resembling that produced by amphetamines. For most subjects the drug served as an appetite depressant. A few had difficulty in falling asleep following the drug experience.

DISCUSSION

The interpretation of results of the Digit Span and Digit Symbol Subtests indicated that even during peak effects of a 75 mg. dose of MDA, there was only a minimal loss in ability to attend, concentrate and perform relatively complex visual-motor tasks. There was no appreciable impairment of visual perception, such as often occurs with LSD or mescaline. Subjects communicated without difficulty and had little trouble making the shift from exploring inner content with eyes closed to responding to the external environment.

Judging from a summation of the impressions obtained from the questionnaire responses and clinical observations, MDA facilitates a state of mind characterized by increased introspectiveness, heightened self-awareness and greater intuitiveness and was associated with emotional states that were described as those of relaxation, acceptance, calmness and serenity. More intense emotional reactions were reported by a few of the subjects. However, they did not feel overwhelmed by, or unable to maintain perspective about their condition. Intense fear and anxiety reactions rarely occurred at this dose level. In some, the drug appeared to induce a state of greater openness in which the individual's responsiveness to music was enhanced and the capacity for rapport and empathy increased. For many of the subjects, the experience took on the overtones of deep personal and philosophical-religious meaning.

Dynamically, the drug seems to reduce the need to defend or aggrandize the ego. In this state of enhanced well-being, the subject seems more able to accept and integrate concepts emanating either from the unconscious or provided by the guide of therapist. In substance, many of the subjects indicated that MDA seemed to "invite" inner exploration in contrast to LSD which "demands" it.

The state of consciousness which MDA facilitates would seem to make the acquisition of new insights an easier process. This type of experience may be especially helpful in breaking through obsessive, anxious and depressive patterns of thought and feeling. Another possibility is its application in group therapy settings to facilitate interpersonal interaction, enhance sensitivity to feelings and possibly promote emotional expression.

Despite this promise, the duration of action of MDA (approximately eight hours) may be a potential draw-

back to therapeutic use. Moreover, the fact should not be overlooked that the compound at one time had had extensive clinical trials as a chemotherapeutic agent in the 1950's when its racemic mixture was studied as SKF #5 (amphedoxamine). Over 400 patients, covering a wide range of psychiatric symptomatology, were treated with this compound in dosages of 10-300 mg. per day. These studies yielded contradictory results, particularly in the treatment of depression, making it impossible to come to any definite conclusions relative to its usefulness as a chemotherapeutic agent.¹⁵ A high degree of variability of reaction was also observed among the participants in the present study who were not manifesting any evidence of a psychiatric disorder. This obviously underscores the need for more intensive scrutiny of those factors that may be playing a role in influencing responsiveness to the drug with the investigative probe narrowed down to the forces that may be creating the variability within the subject. This matter would be of considerable importance in determining the application of this compound in a manner that would enhance its potential as an adjunct to the psychotherapeutic process.

CONCLUSION

It is obvious that the results obtained in this study have limited generalizability. In addition, it was surprising to find the extent of variability in reactivity among this small sample of ten subjects, despite their prior experience with drugs and the efforts to control the set and setting. This variability emphasizes the necessity of obtaining a deeper scrutiny of the factors operating within the individual that determine and influence the major dimensions of response to the drug, an objective that is of critical importance in seeking to employ specific psychotropic effects as useful adjuncts to the psychotherapeutic process. Nevertheless, despite the uncertainties outlined above, there seems sufficient evidence to warrant further study relative to the usefulness of MDA in the context of drug-assisted psychotherapy.

APPENDIX 1

Psychedelic Experience Questionnaire W. Pahnke & W. Richards

I. Internal Unity (Eyes Closed)

Loss of your usual identity.

Freedom from the limitations of your personal self and feelings, a unity or bond with what was felt to be greater than your personal self.

Experience of pure Being and pure awareness (beyond the world of sense impressions).

Experience of oneness in relation to an "inner world" within.

Experience of the fusion of your personal self into a larger whole.

Experience of unity with ultimate reality.

I. External Unity (Eyes Open)

Experience of oneness or unity with objects and/or persons perceived in your surroundings.

With eyes open, seeing something in your surroundings more and more intensely and then feeling as though you and it became one.

Experience of the insight that "all is One."

Loss of feelings of difference between yourself and objects or persons in your surroundings.

Intuitive insight into the inner nature of objects and/or persons in your surroundings.

Awareness of the life or living presence in all things.

II. Sense of Sacredness

Experience of amazement.

Sense of the limitations and smallness of your everyday personality in contrast to the Infinite.

Sense of profound humility before the majesty of what was felt to be sacred or holy.

Sense of being "outside of" time, beyond past and future.

Sense of reverence.

Feeling that you experienced something profoundly sacred and holy.

Sense of awe or awesomeness.

III. Objectivity & Reality

Feeling that the consciousness experienced during part of the session was more real than your normal awareness of everyday reality.

Gain of insightful knowledge experienced at an intuitive level.

Certainty of encounter with ultimate reality (in the sense of being able to "know" and "see" what is really real) at some time during your session.

You are convinced now, as you look back on your experience, that in it you encountered ultimate reality (i.e., that you "knew" and "saw" what was really real).

IV. Transcendence of Time and Space

Loss of your usual sense of time.

Feeling that you experienced eternity or infinity.

Loss of your usual sense of space.

Loss of usual awareness of where you were.

Sense of being "outside of" time, beyond past and future.

Feeling that you have been "outside of" history in a

realm where time does not exist.

Being in a realm with no space boundaries.

Experience of timelessness.

V. Deeply-felt Positive Mood

Experience of overflowing energy.

Feeling of tenderness and gentleness.

Feeling of peace and tranquility.

Experience of ecstasy.

Feelings of exaltation.

Feelings of universal or infinite love.

Feelings of joy.

VI. Ineffability

Sense that the experience cannot be described adequately in words.

Experience of a paradoxical awareness that two apparently opposite principles or situations are both true.

Feeling that you could not do justice to your experience by describing it in words.

Sense that in order to describe parts of your experience you would have to use statements that appear to be illogical, involving contradictions and paradoxes.

Feeling that it would be difficult to communicate your own experience to others who have not had similar experiences.

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