

EXPERIMENTAL PSYCHOTIC STATES

JOHN M. MACDONALD, M. D.,¹ AND JAMES A. V. GALVIN, M. D.,²
DENVER, COLO.

The production of temporary psychotic states by such drugs as cannabis indica, mescaline, and cocaine has long fascinated not only psychiatrists and psychologists but also writers and philosophers. Although systematic psychiatric research on artificial psychoses dates from Kraepelin's work in 1883, addicts have taken such drugs from early times. Cannabis indica addiction is recorded as early as the first century A.D. Mescaline was taken in the form of the cactus peyotl by the Indians in the Aztec era before the conquest of Mexico by Cortez. The Indian use of mescaline to produce ecstatic hallucinatory states for special religious ceremonies was described in 1896 by the anthropologists Prentiss and Morgan. One year later, an account of a mescaline induced psychosis was given by Havelock Ellis(1) but his paper attracted little attention, probably, as Mayer Gross(2) suggests, because it was obviously regarded as the product of an artist writer's wild phantasy. Very dramatic descriptions of experiences under the influence of drugs have been given by De Quincey (*Confessions of an English Opium Eater*), Baudelaire (*Les Paradis Artificiels*), and more recently by Aldous Huxley (*The Doors of Perception*). A graphic account of visual hallucinations experienced during a mescaline psychosis was written by Weir Mitchell(3).

Stars sparkled and passed away. A white spear of grey stone grew up to a huge height and became a tall richly finished Gothic tower of very elaborate and definite design, with many rather worn statues standing in the doorways or on stone brackets. As I gazed every projecting angle, cornice and even the face of the stones at their joinings were by degrees covered or hung with clusters of what seemed to be huge precious stones but uncut, some being more like masses of transparent fruit. These were green, purple, red and orange, never clear yellow and never blue. All seemed to possess an interior light and to give the faintest idea of the

perfectly satisfying intensity and purity of these gorgeous colored fruits is quite beyond my power. All the colors I have ever beheld were dull as compared to these.

The discovery in 1943(4) of the psychic effects of D-lysergic acid diethylamide, a semisynthetic derivative of rye ergot, has reawakened interest in the effects of drugs on the personality. The claim has been made that lysergic acid and other hallucinogens produce a schizophrenia-like state in normal persons. As many psychiatrists today continue to believe that schizophrenia is based on a primary organic pathology, it is not surprising that research on hallucinogens has largely been directed toward a search for a possible biochemical aetiology of schizophrenia. Hoffer, Osmond, and Smythies(5), impressed by the similarity in the molecular structure of mescaline and adrenaline, investigated adrenochrome, a metabolite of adrenaline. They found the adrenochrome produced a temporary psychotic state, but Rinkel and others(6) were unable to confirm these findings. The latter authors believe that adrenoxine, another metabolite of adrenaline, is perhaps the active agent in producing a temporary psychosis. Osmond and Smythies(7) have suggested the possibility that a natural error in the metabolism of adrenaline may give rise to schizophrenia.

The claim that hallucinogens induce a schizophrenic-like state is, however, open to question. The mental state produced by hallucinogens will be considered on the background of experience gained as the result of administration of lysergic acid to a mixed group of 50 psychotic and neurotic patients. In addition, the writers experimented on themselves. The use of lysergic acid in the clinical practice of psychiatry will also be reviewed.

THE LYSERGIC ACID PSYCHOSIS

Remarkably small doses of lysergic acid are required, and in some persons 0.02 mg. is sufficient to produce a psychosis. Psychotic patients are resistant to the effects of the

¹ Assistant professor of psychiatry, University of Colorado School of Medicine; assistant medical director, Colorado Psychopathic Hospital, Denver.

² Associate professor of psychiatry, University of Colorado School of Medicine; medical director, Colorado Psychopathic Hospital, Denver.

drugs and require up to 6 micrograms per kilogram body weight. In the present series, nonpsychotic patients were given 1-3 micrograms per kilogram body weight. The effects appear within $\frac{1}{2}$ to 1 hour, reach their maximum in 2 hours, and may persist for as long as 12 hours. Physical symptoms may include feeling of weakness, dizziness, palpitations, loss of appetite, and nausea. These symptoms seldom cause marked discomfort. Physical signs include elevation of the blood pressure, increased pulse rate, dilatation of the pupils, slurring of speech, and ataxia. One patient with hypertension developed auricular fibrillation which disappeared without treatment within 24 hours.

The most striking feature of the mental state of the lysergic acid psychosis is the wealth of visual disturbances, which were present in 26 of the 50 patients examined. The visions have been well characterized by their lavish colors and more-or-less geometric forms, all of which are in perpetual movement. One patient described seeing Spanish dancers performing, another thought an attendant had horns on his head and hands like claws. A nurse's face was thought to be covered with parallel strips of scotch tape while another nurse looked like Satan. Intensification of colors is frequently noted. Objects perceived may seem to change their form. Anxiety is heightened by the blurred, uneven outline of buildings and faraway objects. The floor seems to be undulating like ripples on the surface of a lake. The walls of the room appear to move backward and forward. A feeling of wide-open spaces may suddenly change to a sense of constriction as the walls and nearby persons seem to close in forbiddingly. There seems to be no limit to the variety of visions that lysergic acid can produce. Illusions similar to those seen in delirium are common, especially when the patient is in a darkened room. One of the writers, while attending a lecture in the evening, 10 hours after taking lysergic acid, was distracted by the sight of peacocks on the carpet and a small scab on the hand gave rise to the illusion that an insect was there. The peacocks and other birds on the carpet were recognized as false perceptions but repeated attempts were made to brush the imagined insect off his hand. Synesthesiae,

for example, visual hallucinations induced by acoustic stimuli, did not occur in the present series.

Auditory hallucinations occurred for the first time in 7 patients, only 2 of whom showed psychotic (schizophrenic) symptoms apart from the lysergic acid experience. Hallucinations of smell and taste did not occur, although loss of sense of taste was commonly present. Almost one-third of the patients suffered severe symptoms of depersonalization, and these were often a source of much anxiety. Disturbances of space perception have been mentioned. Time perceptions may also be distorted. Time may pass very quickly giving rise to a striking sense of urgency. Every request must be attended to without the slightest delay. One patient thought he had been given the drug the previous afternoon. Conversely, time may pass very slowly and complaint may be made of a sense of timelessness.

Sexual excitement is not usually provoked by lysergic acid and occurred in only 3 cases.

Mood changes usually occur in the direction of mild euphoria, especially in the early stages. Patients may make facetious remarks or laugh for no apparent or for inadequate reason. Yet, paradoxically, the patient's statements of well-being or even ecstasy may be accompanied by an appearance suggestive of an acute anxiety state. There may be wringing of the hands, restlessness, or a tense, nervous attitude with a facial expression of great apprehension and fear. The mood though usually euphoric may fluctuate considerably and the patient may become irritable, anxious, fearful, or depressed. Anxiety is commonly present at intervals during the lysergic acid experience and in some cases is the predominant affect. Rarely the mood throughout may be one of depression. Two depressed patients developed severe stupor and in one this persisted until terminated with electrotherapy. Behavior is related to the underlying emotional state.

Increased pressure of speech was noted in more than half the patients while a reduction in speech was present in about a third. Several patients either did not speak at all or made only brief replies to impersonal questions. At the height of the psychosis several patients appeared reluctant to discuss their

experiences. One of the writers found the phantasy world so entertaining that he became impatient when asked to describe it. The experience was too satisfying and the time too precious to be spent in describing this state of ecstasy. He felt he was floating in space, his mind separated from his body, and that he was passing the observers by in space. Furthermore, he thought that the observers, too, were participating in this experience and that it was, therefore, pointless to answer their questions. Several patients complained that their thoughts would suddenly disappear. Perseveration, flight of ideas, increased distractibility with impairment of concentration, difficulty in grasping the meaning of complex statements and incoherence were features of the thought disorders present. These symptoms varied in degree from one patient to another but were more prominent when large doses of lysergic acid were employed. Paranoid ideas were common, even in patients who had not previously shown paranoid symptoms. Frank paranoid delusions rarely occurred except in paranoid schizophrenic patients. One such patient relived a battle scene on Guadalcanal. He thought he was being attacked by the Japanese and he smashed several pieces of furniture protecting himself from his imagined enemies.

Of the 50 patients examined, 21 showed a state of clear consciousness; 12 showed, at times, slight confusion, but were able to concentrate effectively when special effort was demanded; 11 showed slight confusion throughout; 3 showed gross confusion, and 3 were stuporous. Clouding of consciousness, when present, varied in degree and was characterized by disorientation, impaired concentration and attention, incoherent thinking, and difficulty in grasping the meaning of simple statements. Symptoms suggestive of a toxic organic state have been reported by others(4, 8, 9, 10). The lysergic acid psychosis may be terminated by intramuscular injection of Thorazine or intravenous injection of sodium amytal.

Some caution is indicated before drawing the conclusion that lysergic acid induces a schizophrenia-like mental state. In both lysergic acid psychosis and acute schizophrenia, patients experience symptoms foreign to

their previous life experiences. In both disorders, patients find difficulty in describing their peculiar feelings and experiences. It does not, however, necessarily follow that their strange experiences are identical. The low incidence of auditory hallucinations in the lysergic acid experience is in striking contrast to their high incidence in schizophrenic patients. Furthermore, while visual hallucinations may occur in schizophrenia, they do not frequently occur nor is it usual to find the wealth of abnormal visual perceptions that are such a striking feature of the lysergic acid psychosis. The frequent occurrence of visual hallucinations and illusions is suggestive of an acute delirious state, and Stoll(4) is of the opinion that lysergic acid induces an intoxication of the acute exogenous reaction type. The wide variation in clinical pictures that may be induced by lysergic acid is comparable to the variation seen in delirious states. This variation is related to the varying personality and psychological conflicts of the patients tested. In general, the psychotic patients responded to lysergic acid by becoming more psychotic with accentuation of their previous symptomatology. Fresh symptoms, when they appeared, were consistent with the previous diagnosis or suggestive of a clouded state. Nonpsychotic patients responded to lysergic acid by showing an exaggeration of their personality trends. Thus schizoid or cyclothymic traits were seen in a more intensified form or even in caricature. Once again clouding of consciousness sometimes complicated the picture. It is of interest to note the reported reactivation by lysergic acid of the original psychosis, whether it be depression or schizophrenia, in patients whose symptoms have previously been relieved by lobotomy. Previous experience with mescaline is pertinent. When this drug was administered to schizophrenic and delirious patients, it was found that the schizophrenics differentiated mescaline hallucinations from their endogenous sensations whereas delirious patients did not.

It is significant that in the lysergic acid psychosis profound psychic changes may take place with relatively clear consciousness. It would appear that lysergic acid psychosis is not identical in form with any of the known, naturally occurring psychoses. The resem-

blance to a toxic delirious state is greater than the resemblance to schizophrenia.

Clinical experience with hallucinogens provides an insecure foundation for a search for a biochemical origin of schizophrenia. On the other hand, hallucinogens may well prove valuable in the further study of the psychological nature of psychotic processes.

HALLUCINOGENS IN THERAPY AND DIAGNOSIS

Guttman and MacClay(11) recommended mescaline for the treatment of depersonalization. The results have been disappointing as mescaline is able to improve only temporarily depersonalization symptoms insofar as they consist of changes in the surroundings (de-realization) but not of the self. Mescaline and lysergic acid have also been used to facilitate recall of repressed memories particularly past infantile experiences. Sandison(12) claims that lysergic acid is unique in that the recovery of repressed childhood memories is associated with a change of body image so that the patient feels he is transformed into the child he was at the time of the traumatic experience. According to Sandison, the patient can actively describe the age at which he feels himself to be and relives with extraordinary clarity events of emotional significance which occurred at that age. Certainly hallucinogens do aid in the recovery of repressed memories and therapeutic abreaction of past events may be encouraged. In the present series of cases, the clinical impression was that lysergic acid compares unfavorably with intravenous sodium amytal as a means of eliciting repressed memories. In 5 patients subsequent use of sodium amytal was more effective in this regard.

Lysergic acid like other drugs may act as an agent of suggestion. Sloane and Lovett Doust(13) report that a healthy person who was under the false impression that he had been given lysergic acid complained of depression, lability which he likened to alcohol intoxication, restriction of the lateral fields of vision, slight deafness, dulling of smell, feelings of pressure and fever, loss of libido and of sense of time combined with difficulty in thinking and finding correct words! As an aid to suggestion, lysergic acid has obvious drawbacks.

Cattell(14) reported unfavorably on use of mescaline in therapy:

In our material some release of formerly repressed ideation and affect was noted, but this was fragmentary, unpredictable and did not prove useful to the patient. The nature of the mescaline situation precluded the development of transference phenomena in most instances, thus obviating the possibility of analyzing these. The usual drug free defence mechanisms and resistances were altered in the direction of simplification. Therefore, analysis of these, even if possible, might not be particularly pertinent. There is no indication that mescaline can serve any useful therapeutic end as employed in the present study.

Lysergic acid frequently relieves depressive symptoms temporarily but it has not proved of value in the treatment of depression. Sandison(12) reports that lysergic acid is of value in the treatment of obsessional neurosis. Doses of 25 to 400 micrograms were given from 6 to 40 times in combination with skilled psychotherapy. These results have not yet been confirmed by other workers and it is difficult to assess the relative importance of the lysergic acid and the psychotherapy in Sandison's cases.

Drugs that induce a temporary psychosis would need to have undoubted therapeutic effects, not possessed by other drugs or somatic therapies, before they would be generally accepted in psychiatric practice. Satisfactory evidence of such therapeutic properties has not yet been demonstrated.

Although lysergic acid sometimes accentuates the clinical picture it was not of value in aiding differential diagnosis.

PERSONAL EXPERIENCE OF LYSERGIC ACID PSYCHOSIS

The self-administration of lysergic acid or other hallucinogen by the psychiatrist is an instructive but painful experience. Weir Mitchell, following a mescaline intoxication, feared that the temptation to call again the enchanting magic of the experience would be too much for some men to resist. Not everyone who has experienced a drug-induced psychosis would share his opinion. Without danger, the psychiatrist may experience hallucinations, illusions, depersonalization, and other symptoms that he sees in his patients.

Fluctuation in insight was an alarming experience following the self-administration of

a relatively large dose (900 micrograms per kilogram body weight). At the height of the psychosis, insight was lost, yet, apart from symptoms of depersonalization and derealization, the experience was neither frightening nor unpleasant. There then occurred brief periods of awareness of the origin of the symptoms. An attempt would be made to pass on this new insight to others present, but before the explanation could be completed, the subject became aware of a loss of grasp of the situation. The resultant feeling of perplexity and anxiety would be heightened by the sudden appearance of alarm and concern on the faces of bystanders. Then insight would be lost completely and the feeling of anxiety would disappear at the same time. This cycle of events was repeated many times before insight returned permanently. Although each cycle was, in fact, very brief, subjectively it seemed prolonged because of severe distortion in time perception.

The period of partial insight with its accompanying severe anxiety may be analogous to the acute anxiety seen in schizophrenics who temporarily are experiencing a period of doubt as to the reality of their delusional world.

During periods of great anxiety the presence of familiar faces or the perception of nurses in uniform or white-coated physicians frequently served to dispel the anxiety and favor a return to reality. The reassuring effect of these persons was of course lost when they appeared alarmed or concerned themselves. On occasion, some members of the staff would enter the room for some purpose not concerned with the experiment, and their activity, whether to obtain some medication or syringe from the medicine cabinet, served to increase anxiety. These experiences may have some value in regard to the treatment of a near-panic state in an acutely ill psychotic patient.

Another physician present during the earlier part of the test made the following observations:

The subject was sitting in a chair and showed trembling of the lips, dilatation of the pupils, perspiration on the hands and face, and seemed generally to be verging on a panic state. However, any suggestion that such was the case met with denial. In fact, he maintained that he was in a state of bliss and that no one could possibly understand

the wonders that he was going through. He seemed to be acutely conscious of his tenuous grasp on reality and he would grasp the wooden sides of the chair, as if to reassure himself that they were really there and to evaluate just what part they played in his environment. He would grasp the dictaphone handle in order to prove to himself it was real. He remarked often that he was above everyone else in space. He looked out of the window and described a nearby building as merging into itself and floating. He seemed anxious to have people around him and there seemed to be a childlike fear of being alone. He became disconcerted when everyone in the room stopped asking him questions and he appeared to be going farther from reality at these times. At first, when questioned directly about thoughts or impressions, he talked about his feelings of bliss but later became evasive and uncommunicative.

The following record is a description of the lysergic acid experience of one of the writers:

I was very anxious before the experiment. The solution of lysergic acid tasted bitter. After 20 minutes, I began to feel a little drunk, slightly dizzy. An alcohol sponge box lay open on the table 2 feet away from my face, and I sensed an unpleasant, acrid smell of alcohol. The unpleasant sensation remained after I closed the box.

The floor was made of plastic tiles, of a solid background color, with an irregular, colored overlay pattern. These colors, green and red, began to shift about and move, rather like a kaleidoscope.

During these initial experiences the anxiety became frightful. I had the sensation of waves of anxiety, during which I could not speak, but only wait for the wave to pass. I felt as if I were shivering like a wet dog, but was surprised, when I looked at my hands, to see that they were not trembling nor sweating and that their color was normal.

Continuing to look at my hands, I felt they were changed. They belonged less to me. They were elongated, and I thought of hands painted by El Greco. I was startled to discover that I could move one of those thumbs.

I sat in a chair, did not move, and spoke in a fairly connected and correct way, although rather more carefully than usual. Throughout the experiment, I had a strong wish to control my behavior, not to act or speak in an abnormal way. I, therefore, attempted to limit myself to experiencing hallucinations, primarily visual and describing them aloud.

For some time after the floor patterns began to move, other objects were normally perceived. I walked, when asked to do so, with normal coordination. I did not want to walk, however, for fear of incoordination. Later, the walls began to move, waving back and forth as if they were curtains being blown by a wind.

I took great comfort, throughout the experiment in seeing and hearing the physician, a friend, who was conducting the experiment. I was also very pleased when a nurse, whom I like and respect, came briefly into the room. I controlled the wish

tiological factor in some naturally occurring psychoses. Experimental psychoses, however, are not identical in form with any naturally occurring ones although there is resemblance to delirium and, to a lesser extent, to schizophrenia.

Lysergic acid does not possess therapeutic value sufficient to justify its use in psychiatric practice other than on an experimental basis. As a means of releasing repressed material, it is less effective than intravenous sodium amytal. Self-administration of an hallucinogen by the psychiatrist permits subjective experience of psychotic symptoms.

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