The administration of mescaline produces an acute reversible psychosis that consists of diverse psychopathological phenomena usually occurring in a clear setting of consciousness. The effects of the drug in normal subjects have been studied extensively, both clinically and experimentally, by Klüver, Baringer, Guttmann, and Stockings among others. The reactions of mental patients have been described from different points of view by Zucker, Lindemann and Malamud, Guttmann and MacClay, and Rubin, Malamud, and Hope. We have also described our findings in nonpsychotic and psychotic subjects.

The present study follows our earlier investigations, which were recently reported.

The reactions of mental patients have been described from different points of view by Zucker, Lindemann and Malamud, Guttmann and MacClay, and Rubin, Malamud, and Hope. We have also described our findings in nonpsychotic and psychotic subjects.

The reactions of normal subjects were closely studied either through previous psychotherapeutic contact or on a frequent observational basis. Thus, the patients' clinical symptomatology and responses prior to the drug administration were well known.

These 59 schizophrenic patients were subdivided into 3 groups. The first was comprised of 17 patients diagnosed as having the pseudoneurotic form of schizophrenia. Seven of these patients showed obsessive-compulsive and phobic states; 3, phobic-depressive states; 6, anxiety-tension-depressive states; and 1 patient, in addition to anxiety and obsessive manifestations, also displayed hysterical and hypochondriacal features. Many of these patients would have been diagnosed elsewhere as severe psychoneurotics suffering from phobic or obsessive-compulsive disorders. The second group was comprised of 26 schizophrenic patients: 4 paranoid, 3 catatonic, 2 hebephrenic, and 17 mixed or unclassified. Seventeen of these patients showed no deterioration; the other 9, slight deterioration. The third group consisted of 16 schizophrenic patients: 4 catatonic, 5 paranoid, and 7 mixed. All these patients were definitely deteriorated, from moderately severe to severe.

The reactions of this series of schizophrenics to mescaline may be classified under the following headings: (1) physiological symptoms in the autonomic, motor, and sensory spheres, (2) disturbances of perceptual activity, (3) mental content, and (4) emotional alterations.

Most patients showed a vegetative disturbance that was more marked in the first and second groups than in the third. However, many of these disturbances are purely subjective and reporting of experiences was poorest in the third group.

Hallucinations occurred quite regularly under the drug. In the first group 15 patients had visual, 8 auditory, and 2 olfactory hallucinations. In the second group, 22 had visual, 8 auditory, 3 olfactory, 1 haptic, and 1 gustatory hallucinations. In the third group 7 had visual, 2 auditory, and 1 olfactory hallucinations. The predominance of visual hallucinations in schizophrenics corresponds to the same observations made on normal subjects. The low incidence of auditory hallucinations is interesting and in striking contrast to the high incidence of such hallucinations in drug-free schizophrenic patients.

Anxiety increase was the most frequent emotional change in schizophrenic patients under the influence of the drug. Many patients displayed hostility. Depression was not
common and when observed was usually of the agitated type. A retarded depression was unusual. Concern with pre-existent symptomatology was often encountered. Evasiveness, vagueness, and denial were seen frequently. These manifestations were usually present before the drug was given and were reinforced under the drug. In some patients the obsessive-phobic symptomatology, which had been present, disappeared under the influence of the drug. Paranoid manifestations were very frequent. These were reinforced in some of those patients who had paranoid trends prior to drug administration. Paranoid manifestations also occurred as a new symptom in a number of patients, especially in those with the diagnosis of pseudoneurotic schizophrenia.

Some verbalized their mental content more openly than before, and memories pertaining to childhood or early life were revealed. However, this was not too common. Sometimes patients released material not previously verbalized, e.g., fear of insanity or ideas of genital inferiority. Occasionally a patient relived actual traumatic experiences. All these manifestations were spontaneous. Some of the patients in the pseudoneurotic group, who had received psychotherapy for relatively long periods, disclosed some new material under the influence of mescaline. Some authors, and especially Stockings, have remarked that mescaline intoxication could be described as a "condensed psychoanalysis." The exact meaning of this is not clear. In a few instances, material with intense affect was verbalized of which the patient was not aware prior to the injection of the drug. There may be a relatively free flow of thought as the patient recounts what he is experiencing, but often we noted refusal to speak, blocking, inability to describe the strange experiences, or merely constricted, repetitious productions. It is not easy for us to see striking parallels between the mescaline experiment and psychoanalysis.

Sexual material occurred frequently in the productions of the schizophrenic patients under the drug. This is especially striking because normal subjects do not usually verbalize much sexual material. Mescaline is not a sexualizing drug in normals. We would like to relate a few samples of such content. One patient talked about his penis being wet, small, or absent, and that he had breasts like a little girl. A female patient went through the experiences of childbirth. Another female patient talked of being raped and especially of being raped under water. Still another female patient went into a state of sexual ecstasy with memories and fantasies illustrative of practically all heterosexual and homosexual activity. She also expressed the desire to become a man, of swallowing the doctor's penis, and of its transformation into a baby. Another female patient recalled earlier sexual desire for her father. Quite a number of patients expressed sexual wishes, fears, inferiority feelings, fear of anal rape, early childhood memories, etc. Much of this material was a repetition or an elaboration of productions in a drug-free state.

Normal subjects and schizophrenic patients under the drug showed both similarities and dissimilarities in their reactions. The vegetative changes—pupillary dilatation, nausea, and vomiting—occur in normals and psychotics. The visual hallucinations, illusions, and distortions of body image occur in both. The content of the perceptual changes appears to be roughly comparable in both groups. For instance, the form of visual hallucinations is the same. The alterations of time sense, unreality feelings, and thought-language changes are similar. In the emotional sphere, occasional depression and frequent paranoid manifestations are seen in both groups. The hebephrenic and catatonic pictures produced in normals are also similar to those seen in schizophrenics.

Nevertheless, there are differences between the reactions of normals and schizophrenics to the drug that must be noted. For instance, the euphoria occurring in normals is stressed by all investigators. Euphoric manifestations were occasionally observed in our schizophrenic patients, but were very much in the background. Sexual content and behavior are frequently encountered in schizophrenics under the drug; these are rare among normals. Generally speaking, the reactions of schizophrenic patients to the drug are much more intense; anxiety is more marked, and disorganization of thought and emotional patterns is very probably more common and intense than in normals, but we are not yet
prepared to say whether these differences are also qualitative. We feel, however, that quantitatively the reaction to the drug is more marked and is associated with more disorganization in schizophrenics than in normal individuals. The normal individuals retain a better reality control, remain more as observers of the various perceptual changes, than actually living in them. It is our impression that, even though many symptoms produced by the drug in normals resemble those of schizophrenia, they are not exactly the same; whereas, in schizophrenic patients, the drug reinforces the schizophrenic symptomatology and magnifies it.

There is also a difference in reaction between patients who have a schizophrenic illness on one hand, and normal individuals and schizophrenic individuals under the influence of mescaline on the other. For instance, in schizophrenics who are not mescalinized, geometrical forms of hallucinations are uncommon, but do occur frequently in normals and schizophrenic individuals under mescaline. The unreality experiences are more directly related to altered perception in both normals and schizophrenics when they are under the drug. This is not seen as clearly in nonmesclainized schizophrenics. The same is true regarding alterations of the body image.

We also made investigations with lysergic acid, a drug introduced by W. A. Stoll in Switzerland, and since applied by other authors. This drug is a synthetic amide prepared from natural d-lysergic acid and diethyl amide, and belongs to the ergobasine group. It was found that lysergic acid does not produce classical organic psychotic pictures, but in very small amounts brings on clinical symptoms similar to those seen in the functional psychoses and especially in schizophrenia. This rather specific mental picture was induced repeatedly and uniformly in normal individuals.

The action of lysergic acid is of great interest because it is chemically different from mescaline, which produces similar symptoms, and because the symptoms are brought on by the oral administration of exceedingly small amounts of this substance.

The solutions of d-LSD-25, which were given us for experimental purposes by the Sandoz Pharmaceutical Company, contained either 20 or 100 gamma per cc. The experiments in the literature were usually carried out with 30 to 40 gamma of d-LSD-25. Usually one-half to one hour after taking the drug, the patient begins to show symptoms that reach their peak after 2 hours, and then the drug action begins to decline. The whole action lasts from 4 to 6 hours, after which the patient usually returns to his original state.

In normals d-LSD-25 produces vegetative symptoms—nausea, malaise, headaches, dizziness, palpitation, dilated pupils, sweating, and diuresis. The blood pressure is reduced, and at times bradycardia is present. A number of patients show ataxia; the Romberg sign is positive; speech is somewhat dysarthric, and forced laughing is also seen. Perceptual changes are in the foreground. Illusions and hallucinations are very common. Geometrical figures, light, and brilliant colors are usually seen. These hallucinations and illusions are very impressive to the subject. Hyperacusis is noticed, but auditory hallucinations are rarely present in normals. Despite the unpleasant vegetative manifestations, many persons who take the drug feel a comfortable lassitude and euphoria. They show a tendency to disinhibition with an increased psychomotor activity and flow of speech. At times lability of affect and depression are also noted.

Our investigations were concerned mainly with the reactions to lysergic acid of patients suffering from schizophrenia, and especially from the point of view of comparison with mescaline effects.

To date, 21 patients have been studied. Some have received the drug repeatedly. Nineteen of the 21 patients also received mescaline, 16 by intravenous and 4 by the oral route (both routes at different times in one patient). The dosages of lysergic acid used varied from 10 gamma to 120 gamma.

Mental changes in our patients occurred mainly if 60 or more gamma were used; below 60 gamma, and sometimes even over 60 gamma, we found the symptoms produced to be unreliable. The 21 patients were all diagnosed as suffering from schizophrenia: 5 pseudoneurotic, 12 mixed, 2 catatonic, and 2 paranoid. Of these patients, 15 showed no deterioration, 4 mild, 1 marked, and 1 severe
deterioration. The vegetative, autonomic, motor, and sensory disturbances in our patients were chilliness, headache, trembling, flushing, pupillary dilatation, numbness of hands, sense of heat, nausea, vomiting, unsteadiness, and hyperacusis. The symptoms occurred 30 to 60 minutes after ingestion of the drug and were very similar to those reported in the literature in normals. The symptoms were also quite similar in the same patients when they received mescaline. The difference, however, in response to lysergic acid was that the changes were less intense and less diffuse than with the intravenous administration of mescaline, but comparable in intensity with the oral use of mescaline. The perceptual disturbances associated with lysergic acid included hallucinations and illusions of the personal and nonpersonal environment and somatic disturbances.

Visual hallucinations with lysergic acid occurred with a significantly lower frequency than with mescaline. The other perceptual disturbances occurred with about the same frequency. In general, the content of the visual hallucinations—geometrical figures, colors, inanimate and animate objects—were the same with both drugs. In some cases the same types of perceptual disturbances occurred with both drugs in the same way. Somatic disturbances were more diffuse and intense with mescaline than with lysergic acid. The time sense was affected in the patients with lysergic acid similarly as with mescaline. In the majority of cases the disturbance was a slowing of the subjective recognition of the flow of time. Unreality feelings were experienced by the majority of the patients with lysergic acid, similarly as with mescaline, but these feelings in general were much less intense with lysergic acid. In the majority of cases the unreality feelings were referred by the patients to disturbances of perception. This was characteristic of both drugs. Disturbances in thought and language processes occurred in every patient receiving lysergic acid when the doses exceeded 10 gamma. This incidence was comparable under mescaline. The most frequent complaint associated with lysergic acid intoxication was a sense of impaired concentration or thinking ability. Patients often related this to a haziness of mind and the sedative-like effect of the drug. Patients sometimes commented on a therapeutic aspect of the sedative-like effect. In some of the patients, speech tended to become slow, sluggish, and slurred, similar to the response to an intravenous barbiturate. Two subjects commented on some pressure of thought in addition to a sense of muddled thinking. None of the patients who suffered from the pseudoneurotic form of schizophrenia showed a frank schizophrenic thinking disorder with lysergic acid (or with mescaline). In some of the overt schizophrenics, however, thinking disorders became more marked, such as increased evasiveness, blocking, scattering, and irrelevance. However, in patients who became quite anxious, the stream of thought showed the usual concomitants of anxiety, with increased or decreased verbal productivity and constriction of content. Emotional disturbances were very common under lysergic acid. Seven patients responded with relaxation, drowsiness, and euphoria. In some patients these mental changes were mixed with increased anxiety. Six patients were depressed with retardation. Three patients showed alternating euphoria and depression, and 6 patients had a predominantly anxious reaction. Associated with the anxiety were irritability, resentment, and a suspicious attitude. Frank paranoid delusional constellations were quite infrequent as compared with the responses to mescaline. Two patients exhibited an intensification of catatonic manifestations and 1 paranoid patient showed a more intense paranoid attitude. No significant effect occurred in 3 patients. Similar reactions of the same patient to both drugs were in the nature of anxiety, coupled with irritability, resentment, and suspicion. The depressive pictures were also very similar. The intensification of catatonic and paranoid pictures was essentially the same. Dissimilar reactions of the same patient to the 2 drugs were attributable in part to a relative absence of effect with lysergic acid, which, however, may be the result of the route of administration. The mescaline was used mainly intravenously and the lysergic acid orally. Therefore, the symptoms occurred in response to mescaline more rapidly and massively, and more gradually and less intensely with lysergic acid. The
euphoric reactions that were present in response to lysergic acid were not present in the same subjects with mescaline. The majority of patients, under the influence of lysergic acid, failed to produce new material. We have used mescaline and lysergic acid, or both, in all 3 groups of schizophrenic patients in whom mescaline or lysergic acid, or both, were used, the well-preserved first group of pseudoneurotic schizophrenics and the second group of undeteriorated or moderately deteriorated overt schizophrenics showed the more intense overt emotional reactions to the drug. In the third group of severely deteriorated schizophrenics, the emotional response was at times intense, but often no content was verbalized and gross cata-tonic withdrawals ensued. The physiological alterations, especially the vegetative ones and the perceptive alterations, like the visual hallucinations, were quite often as intense as those seen in the first 2 groups.

The question arises as to the consistency of the response of a given person if exposed at different times to the drug. On successive occasions the response to the drug, of course, is a very complex issue and depends on many physiological and psychological factors at a given time. It was assumed by some that in many patients the response to the drug would be different from time to time and that the patient would adapt himself to the experiences under the drug and become less responsive to it. In some of our patients these alterations in response actually occurred. In the majority of the patients, however, with the exception of decreased anxiety, tension, and unreality feelings, such manifestations as paranoid attitudes, silliness, schizophrenic thinking disorders were often reproduced with the same intensity as before. Often more euphoria was noted on repeat administrations. We have found that schizophrenic patients retain the basic pattern of response to repetition of mescaline. This is clearly illustrated by patients to whom the drug was given before and after topectomy. After topectomy the reactions were often very similar as before, even in those patients in whom postoperative improvement or recovery took place. Mescaline was able to reactivate the psychosis in every detail after the operation. In some patients the quantity of the response was reduced.

We have used mescaline and lysergic acid essentially for investigative purposes. Both drugs are very important in producing schizophrenic-like reactions in normal individuals, in magnifying the schizophrenic structures in schizophrenic patients, and in studying the personality structure of different individuals under drug stress. Through the use of these drugs we believe that valuable contributions can be made to the understanding of the organic and functional psychoses. We have attempted to use these drugs for diagnostic, prognostic, and therapeutic purposes. We do not believe that the evidence available today would permit their reliable use for any of these clinical approaches. It is undeniable that the drug precipitates an overt schizophrenic psychosis in some individuals in whom pseudoneurotic schizophrenia is diagnosed. However, these overt psychotic responses produced in pseudoneurotic schizophrenics will have to be qualitatively and quantitatively differentiated from schizophrenic-like clinical pictures in so-called normals under the drug. We feel that in a number of instances we are able to differentiate between schizophrenic-like responses in normals and overt psychotic reactions in pseudoneurotics, but not invariably. Therefore, further investigations in this field are warranted.

Mescaline has also been used by some investigators, just as sodium amytal, pervitin, and other drugs have been used, to accelerate psychotherapy or to obtain psychodynamic material not otherwise available prior to the drug treatment. We have mentioned that some of our patients revealed new material under the drug. However, in many patients whose psychodynamic structures had been well investigated prior to the drug experiment, nothing new was learned. The extent to which mescaline and lysergic acid will be of use in therapeutic work must be ascertained in a study of a large number of patients. Further investigation is certainly indicated. It is possible that mescaline, like amytal and other drugs, can also be used for prognostic purposes. Deteriorated schizophrenic patients apparently respond differently to the drugs than do well preserved schizophrenic patients. It is possible that regressed patients have a different reaction...
to it than deteriorated patients, but our knowledge here is still very scant. The differences in the responses of various schizophrenic patients would indicate that many variables enter into the reaction of a schizophrenic patient. It is impossible, today, to establish a common denominator in all the responses of these patients to mescaline and lysergic acid.

**SUMMARY**

The effects of mescaline and lysergic acid were studied in schizophrenic patients. It was found that physiological changes were produced in these patients and that mental symptomatology was markedly aggravated. The observations made with the above-mentioned drugs on normal individuals were compared with those seen in schizophrenic patients. Mescaline and lysergic acid are drugs that disorganize the psychic integration of a person. This disorganization is much more apparent in schizophrenics than in normals. The diagnostic, prognostic, and therapeutic use of these drugs is also discussed.