LYSERGIC ACID DIETHYLAMIDE (LSD-25)

A Clinical-Psychological Study [1]

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Introduction

A study has been made of the effect of lysergic acid diethylamide (LSD-25 Sandoz or LSD) on the affect, cognition, and expression of "normal" control subjects and of depressed patients. It has already been shown by Stoll(1, 2) that LSD has a pronounced psychic effect, manifested by increased emotional lability, dissociation, and imagery. Stoll described a euphoria that LSD occasionally produces in mental patients. It is the purpose of this present study to determine if such a euphoria might be of value in the treatment of depression.

Studies were done on 20 subjects, 5 "normal" controls and 15 depressed patients. (The sole criterion of "normalcy" was that the individual function adequately in his immediate life situation.) The "normal" controls were each given a single oral dose of 20 micrograms before breakfast. Psychological and physiological observations were carried out over a period of 8 to 15 hours.

The depressed patients were started on an oral dose of 20 micrograms, which was increased daily to a point where a definite psychophysiological effect could be observed. This point varied in different patients from 20 to 100 micrograms. Psychological and physiological studies were carried out before, during, and after the course of treatment with LSD. Treatment covered a period of a month except where it had to be interrupted for medical reasons.

Results

A. *Studies on Normal Control Subjects*

A sample protocol follows.

0600 R 18, P 60, BP 90/70. Subject took 20 gamma orally.

0630 R 17, P 65, BP 100/74.

0700 R 16, P 70, BP 104/74.

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0800 R 14, P 68, BP 104/76. He reports numbness and tingling of legs. Tendon reflexes are increased.

0830 R 20, P 73, BP 104/84.

0900 R 20, P 68, BP 118/100. He laughs incontinently, uses language immoderately, and shows flight of ideas.

0930 R 24, P 65, BP 120/100. He complains of paresthesias and distortions of vision; the contour of objects appears fluid.

1030 R 12, P 80, BP 104/76. He complains of "wolves howling," and reports hallucinations on closing eyelids.

1100 R 14, P 80, BP 104/76. He recites limericks and laughs at his own humour.

1205 R 18, P 70, BP 130/94. Mydriasis is marked.

1345 R 19, P 68, BP 120/96. Pupils now 5 mm. and react slowly to light and accommodation. He complains of sirens, tuning whistles and Morse code, and compares their intensity with that of a motor audible in the vicinity. (There was then no motor running.) He sees brightly coloured birds and hears them singing. He complains that blood pressure cuff causes extreme pain. He then complained that the drug had transformed him into a "television set," because the paresthesias in his face and extremities seemed identical with the ripples and fadeout of the television screen. He believed that through this drug one could control others by sending out impulses that would be picked up by whoever took the drug. Subject was unaware of the bizarre nature of this idea.

1540 Pupils still dilated. Subject complains that couch is moving in time with his heart beat.

1700 Pupils 4 mm. Visions are decreased but bright figures on dark background are still reported. He hears the "Three-Cornered Hat."

1800 Sleeping.

2100 R 18, P 62, BP 120/84. Pupils 3 mm. Subject claims that he feels fine and clear-headed and appears so objectively.

Résumé of other control subjects: only 2 of 5 reported vivid hallucinations and euphoria as described above. The others manifested extreme tension and anxiety.

B. *Characteristic Effects of Lysergic Acid Diethylamide (LSD-25)*

Description is given of the effects of LSD in the order of appearance. This order is subject, however, to individual variation. Effects

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are noticed ½ to 1½ hours after oral administration. They usually last 4 hours, but sometimes as long as 12 hours. None of these effects could be noticed if, unknown to subjects, water was substituted for the drug.

Autonomic nervous system: The initial reaction is like that of known sympathomimetic drugs. There is a rise in blood pressure and pulse rate, occasionally followed by a rapid drop in both blood pressure and pulse. Mydriasis and cycloplegia are present. Changes in respiration are variable.

Subjective symptoms are initiated by numbness, faintness, headache, neckache, and tension. Paresthesias come in waves. Nausea may occur; appetite is indifferent. There is a sense of urgency.

Motor system: Following the onset of paresthesias, psychomotor difficulties are apparent. Initially there is a fine tremor, increased by voluntary movement. This is followed by incoordination. Subjects may have difficulty in walking and difficulty in standing in Romberg's position. Fine movements are more difficult and handwriting becomes larger, more cumbersome, more childlike. The tendon reflexes are increased but no pyramidal signs are noted.

Mood: As the subject becomes adapted to the novel sensations and motor impairment, euphoria may ensue. There is a sense of aggrandizement, a feeling of omnipotence, but euphoria is not always present. Some individuals find the distortion of reality too threatening, and instead of euphoria there is a heightened anxiety, a desperate holding on, and an effort to maintain control of the situation, together with a heightened suspicion of the motives of others and hypochondriacal concern over the above symptoms. One person complained it was like being caught in a burning building; another that it was like going under ether; a third that it was like hanging over a cliff. Affect may be dissociated from experience so that the emotional reaction is inappropriate to the situation or to the content of thought.

Conation: LSD gives the subject an increased feeling of energy. He forms ambitious designs. The impairment of vision, and coordination, the rapid flight of ideas, the failure of reality testing make executive action difficult.

Cognition: The changes in mental activity are characterized by flight of ideas, difficulty in concentration and in coordination. Nevertheless, results on the Wechsler-Bellevue Test showed no significant difference. Memory and comprehension are in no way impaired. Loss of "reality testing" is exemplified by subject who carried on conversations with a Szondi card. Attempts were made to test subjects before they were handicapped by failure of accommodation, and this is perhaps sufficient explanation of the failure to show a significant deficit. Apparently distortion, rather than deterioration of mental function, takes place.

Sensorium: Alterations in the sensorium follow or may coincide with the euphoric state. Initially this may appear as a heightened sensitivity and the subject may notice things of which he was not previously aware, such as a gold tooth in the mouth of the examiner. Defects in the surroundings appear exaggerated. Noises become unbearably loud. Minor physical discomforts become the center of attention. This stage is followed by a distortion of reality. Illusions are frequent and often disturbing. The walls seem to pulsate and melt and they may apparently teem with insects. Distortions are present in all sensory modalities: a motor running may be heard as a symphony; the pulsations of the temporal artery are interpreted as movements of the pillow; a glass thermometer tastes like rubber; water tastes as though it had salt in it. Most striking are the hallucinations that succeed the illusions, most prominent in the visual field. Usually, unformed lights are first seen, followed by formed images such as brightly colored figures on a dark background. Geometrical figures are succeeded by human figures and human faces and scenes. These figures are of extraordinary plasticity, and change and multiply so that, if one sees a face, it may be reduplicated one-hundredfold. The rapid change of one image to another is illustrated thus: a subject heard a noise that suggested a mouse running about. He saw an image of a mouse caught in a trap, its tail curled much as in Straub's test. The S-shaped outline of the tail formed in turn the outline of a woman's body. Within each circle outlining the woman's breasts

appeared a face. The faces multiplied rapidly to fill the entire field of vision.

On another occasion the thought of food gave rise to the hallucination of a cabbage followed in turn by a knife and fork. Auditory hallucinations are frequent and may occur simultaneously with the visions so that a choir may be seen and heard. Train whistles and sirens are common; spoken words are heard rarely. Hallucinations of touch, taste, and smell are often present but are less vivid. The transition of images into hallucinations can be observed. Within the after-image of a light bulb a face may appear. This hallucination appears to obey Emmert's law. Hallucinations may be induced by suggestion. One subject was asked to listen to the Scheherazade. Instead he heard the Three-Cornered Hat initially, and only later could he hear the suggested music.

Another subject demonstrated the autosymbolic phenomenon. Asked to concentrate on smoothing out a piece of work he had done, he saw a vision of a woman smoothing out a wrinkled bed. The folds in the bed became larger and turned into ocean waves on which appeared an ocean liner.

Certain resemblances to the dream state may be pointed out. As in the dream, sensory stimuli may be translated into images or hallucinations. As in the dream state, thoughts are translated into images and images into thoughts. Hallucinations often represent a condensation of previous experiences. One subject having seen a cardinal (Richmondena cardinalis) reported a vision of a masked bandit prowling around Fifth Avenue. The black markings suggested a mask and the mask a bandit so that the bird was seen as a bandit.

These findings support the conclusions of Stoll that LSD produces an "intoxication of the acute exogenous reaction type" with vegetative and motor symptoms and impressive disturbances of mood, stream of consciousness, and perception leading to an eidetic state.

C. *Therapeutic Results with Depressed Patients*

Studies were made on psychiatric patients to determine if LSD would produce a euphoric state that would be of therapeutic value and if it would serve as an aid to interview-psychotherapy. All severely depressed patients of whatever diagnostic category admitted to the hospital were studied extensively. After a period of observation some were given a course of LSD usually of a month's duration. Follow-up studies were continued for about 6 months after treatment. An effort was made to match each depressed patient so treated with another patient comparable as to age and psychopathology who received no specific treatment. All patients treated with LSD were blocked and inaccessible before treatment. Some representative case studies follow:

CASE 1.—This patient is a 55-year-old entrepreneur admitted with the complaints of nervousness and palpitations. On medical examination evidence was found of persistent hypertension ranging around 210/130 with concomitant beginning retinopathy, mild anemia (hemoglobin 90%). He was moderately obese, weighing 176 pounds but otherwise his physical condition was not remarkable. The patient complained that "life was no longer worth living." He felt discouraged and depressed. On psychiatric examination he appeared blocked, retarded, confused, tearful, and depressed. Formerly, he had a good business and a good home. Of late he had spent most of his time drinking, until he found himself homeless, friendless, and penniless. Diagnostic impression was involutional psychosis. He was considered a suicidal risk. Projective studies revealed heavy repressed dependent needs, obsessive trends, and reliance on psychosomatic solutions. Hospitalization alone had no ameliorating effects nor was he accessible to psychotherapy. He parried all efforts by a rambling, persistent, circular discourse. In meaningful areas he was blocked. As he had experienced no improvement after 7 weeks' hospitalization a trial of LSD was initiated. The initial dose was 20 micrograms daily, which was gradually increased to a maximum of 60 micrograms. Dosage was continued over a 4-week period. Mild euphoria was frequently noted and this effect was sustained after the obvious physiological reaction had worn off. He improved for about a fortnight. Then he began to suffer occasional distressing symptoms consisting of shortness of breath, headache, tinnitus. He complained of feeling "jittery and nervous." These symptoms were usually associated with marked feelings of hostility evoked during treatment. They disappeared after these hostile sentiments had been openly expressed. After expression of feelings of resentment he would usually experience euphoria during the following treatment day. Neurological signs during treatment were limited to mydriasis, ataxia, and incoordination. His sensorium remained clear. After one week he remarked that he was feeling better than he had in months. He became less seclusive and socialized readily. His

blood pressure fell to around 190/110, a result explainable by increased rest and decreased tension. His weight increased 2 pounds. His hemoglobin fell to 80%, and a blood smear showed toxic granulations. Initially, his spontaneous productions were unchanged. Only after considerable symptomatic improvement had taken place was the patient able to verbalize considerable hostility toward his family. Hitherto, his drinking and failures in work had been his only means of expressing resentment. Thereafter, he not only felt better but was able to carry out plans for employment and reconciliation with his family. His dependence was in no way overcome but he had obtained a better recognition of it. Rorschach and Szondi studies during treatment revealed no basic personality changes, although he appeared more constricted and defensive. After therapy these studies showed an awareness of dependent needs but also some decrease in these latent needs. There were increased adaptivity, a mood upswing, and increased drive. He was optimistic about his recovery, remarking, " I don't know what you did but it was wonderful." He was discharged as recovered, 2 months after onset of LSD therapy.

CASE 2.—This patient is a 20-year-old, unmarried male who was admitted to the hospital in an acute depression with the complaint of nervousness. He was quiet and volunteered little. He complained tearfully that his mother was about to lose her home, his sister her job, and that he had to do something about it. He felt depraved and useless, and thought life was not worth living. He was both combative and suicidal. Marked resentment to the mother was considered of etiologic significance in the development of the depression. Physical condition was good. He weighed 156 pounds. Hemoglobin was 100%, urine was negative, blood pressure was 125/80, and pulse was 68. Because of his depression he was placed on a course of LSD for a month. No therapeutic effect was observed with doses as high as 100 micrograms. Occasionally he was fluent but usually he remained blocked. Once he complained that he was 3 inches high and that others might step on him. But usually no changes in sensorium could be elicited. He did not improve but continued withdrawn and depressed. He lost 10 pounds in weight. His hemoglobin fell to 90%. Final diagnosis was schizophrenic reaction, chronic depression, unimproved.

CASE 3.—This patient is a 35-year-old unmarried lawyer admitted to the hospital after a serious suicidal attempt by poisoning. On admission he was considered depressed and suicidal even though he glossed over the depression with bland avoidance of personal problems. His physical condition was good after he had recovered from his suicidal attempt. His blood pressure was 138/60, pulse 80, weight 180, hemoglobin 100%. He was given from 20 to 70 micrograms of LSD daily for a 4-week period. During this time no neurological signs were present. Blood pressure changes were minimal. His weight did not vary. Occasionally he complained of distortions of vision, noting that other people appeared squat and shorter than himself. Free association to this distortion revealed to him his feelings of isolation and a compensatory need to feel superior to others. During his initial treatment he felt tense, anxious, and upset, but he was able to express some appropriate feelings of anger. Up to that point he had been unaware of his resentments. Now he came to view his relations with others more realistically. After 3 weeks he became less defensive and reacted and spoke more in terms of his real feelings. He gradually became aware of the role of hostility in the ontogenesis of his depression. Although repressed affect was elicited during LSD therapy, and although his depression cleared up, his basic personality remained unchanged. During severe stress he reverted to alcohol. However, his depression did not recur. Final diagnosis was schizoid personality with depressive reaction. He was discharged as improved 7 months after his admission.

DISCUSSION

Fifteen patients with severe depressive reactions were treated with LSD. Two suffering from involutional psychoses made complete recoveries to their prepsychotic state. Four suffering from schizophrenic reaction with depression showed no change or became worse. Five schizoid persons with severe depressive reaction improved so that they became free of depression; basically, they remained schizoid. In 4 other cases treatment was interrupted. Of these 4, 2 developed profound circulatory depression, which required termination of treatment. The other 2 were diabetics who were transferred to the medical service before LSD treatment was completed. Curiously, their insulin requirement was lowered temporarily after taking LSD. The validity and meaning of this observation are as yet uncertain.

By contrast in the control series of involutional psychoses, 2 patients recovered without specific therapy. Of 4 schizophrenic patients with depression, 1 signed out against advice, unimproved; the others were transferred to mental hospitals, as unimproved.

Of 5 schizoid patients with depression, 3 showed improvement on hospitalization alone, while 2 failed to show improvement. Within the limits of this sample, LSD does not appear to have a significant therapeutic advantage in depressed states, although it appears of value as an adjuvant in a certain number of cases. It has the disadvantage of increasing an already present anxiety. It

has other disadvantages. The anorexia it produces may accentuate weight loss. There is some tendency for anemia to appear after prolonged dosage, although this may be referrable to reduced food intake. Insomnia is often aggravated.

The effect of LSD is too disorganizing for ambulant patients. With 2 patients it seemed to foster a better doctor-patient relation by enabling them to express and recognize feelings. Only one patient was able to discuss his difficulties more freely during a pronounced euphoric reaction.

About half the patients developed lessening of depression, improvement of mood followed by clinical recovery from the depressive reaction, but unless this improvement was followed up by psychotherapy patients had difficulty in maintaining improvement.

These data appear in keeping with Condrau's(3) observation that no definite conclusions can be drawn as to the diagnostic and therapeutic value of LSD.

The possibilities of personality explorations through direct communication envisioned by Stoll were not realized. While LSD was not of value in promoting free verbal exchange, it is of potential use in personality exploration by the analysis of the hallucinations that it produces, as in the following example:

One patient reported a colourful mediaeval pageant and made a sketch of it. After the effects of LSD had worn off, the sketch was presented to the patient who at first could make nothing of it. On free association, the patient brought up the idea that the mediaeval figures were really psychiatrists, with whom the patient had been associated. One figure was drawn with an open door for a mouth and a window for the one good eye. This psychiatrist talked too much and saw only half of the patient's difficulties. Another figure drawn slant-wise or leaning was considered a drunkard. A third was pictured as a knight with visor drawn both open and closed. Associations to this drawing suggested that the psychiatrist was two-faced. A fourth armour-clad figure was in reality a female, suggesting that he was effeminate. The mediaeval setting with its rich pageantry and hapless figures suggested the ambivalence and disappointment about psychotherapy. Thus neither patient nor psychiatrist was left in doubt as to the patient's negative feelings, which had previously gone unrecognized.

By contrast projective testing during LSD intoxication was less revealing than that done during the normal waking state. All patients and all but 2 controls showed marked constriction in the Form-Interpretation test. It was inferred that the patient attempted to compensate the effects of LSD by an increased effort at control.

Summary and Conclusions

Lysergic acid diethylamide (LSD-25 Sandoz) given orally in single doses as low as 20 micrograms produces depersonalization, derealization, and increased imagery in "normal" individuals. Larger doses are required to produce the same effect in psychotic patients.

Of 15 patients with depressive reactions, 3 recovered and 4 improved after one month's treatment with daily oral doses of 20-100 micrograms of LSD. Four patients showed no improvement. In 4 cases, treatment was discontinued before proper evaluation could be made. Anxiety was a prominent reaction while less frequently euphoria was observed. In 3 patients who developed euphoria it served as an aid to psychotherapy by encouraging expression of feeling. In the others the heightened anxiety encouraged reticence rather than confidence.

Improvement obtained during the course of LSD therapy was not greater than that obtained without its use in comparable cases. However, LSD affords therapeutically valuable insights into unconscious processes by the medium of the hallucinations it produces.

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