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LONG-TERM PSYCHOLOGICAL EFFECTS OF LSD [1]

SPENCER A. McWILLIAMS [2] AND RENÉE J. TUTTLE

University of Arizona

The literature reporting lasting adverse psychological reactions to LSD is reviewed, along with other relevant reports where LSD users were followed. The danger of long-lasting psychological damage is low when the drug is used by emotionally stable individuals in secure, controlled settings, but persons with psychiatric disturbance, unstable personalities, and current crisis situations have experienced pathological behavior temporally related to drug ingestion. Adverse reactions were not reported in well-controlled studies with normal subjects, indicating the drug's relative safety for continued research.

Although lysergic acid diethylamide (LSD) was discovered to have hallucinogenic powers in 1943, drugs with similar makeup and pharmacological effects have been used for many years, especially by American Indians in their religious rituals (Pelner, 1967). Since the synthesis of LSD, these drugs have become a subject of empirical study among behavioral scientists studying the effects of such agents, their purported ability to induce schizophrenic states, and their use in psychotherapy. During the 1950s a number of research projects investigating the clinical effects of LSD were undertaken (See Cohen, 1967; Cole & Katz, 1964; Freedman, 1968, 1969; Ludwig & Levine, 1966; Osmond, 1957; Unger, 1963, for reviews).

Many laymen became aware of the reported ability of LSD to induce altered perceptual states and intense positive personal experiences (e.g., Huxley, 1954). This "psychedelic" orientation (Osmond, 1957) led to use of LSD in the general population, particularly among the young. Although long-term reactions to LSD had occasionally been reported from medical administrations (Cohen, 1960), the increasing nonmedical usage prompted warnings about the possibility of adverse psychological effects resulting from LSD usage.

A pamphlet distributed by the State of New York warned that LSD can precipitate an acute psychotic episode, requiring extensive treatment and from which some persons may never recover (Narcotic Addiction Control Commission, 1968). Grinker (1963, 1964) warned against the use of LSD unrelated to scientific research and criticized the results of LSD therapy suggesting that LSD could induce harm. Louria (1967) associated use with liberalization of morals and permissiveness and criticized LSD because its users withdraw from productive activities in society. He reported that many patients were hospitalized with psychoses induced by LSD. Largely because of such warnings, possession of LSD is now illegal, and research on its pharmacological effects and use in psychotherapy has decreased.

The issue is a controversial one, however, and not all authorities agree with the above conclusions. Hollister (1967) stated that LSD does not induce permanent psychosis and explained that the reported psychoses were due likely to the attraction of such drugs to people who are already emotionally disturbed. Freedman (1968) concurred and said that a causal relation between emotional disorder and LSD

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[2] Requests for reprints should be sent to Spencer A. McWilliams, Department of Psychology, University of Arizona, Tucson, Arizona 85721.

usage was not justified simply by the presence of emotional turmoil in concurrence with the drug.

The unfavorable publicity surrounding LSD usage has hampered research efforts. Dahlberg, Mechanek, and Feldstein (1968) surveyed 29 investigators doing research on LSD-type drugs. The 19 who responded indicated that unfavorable publicity made it difficult for them to recruit appropriate subjects and caused pressure to discontinue research with the drug. Mogar (1968), in announcing his decision to withdraw entirely from research with psychedelics, discussed what he considered an oppressive social climate surrounding the drugs, which hindered the investigator. He felt that prevailing attitudes made creative and objective research difficult, and open and rational discussion of the drugs was hindered because of biases generated by sensationalism and controversy. Because of the illegality of the drugs, subsequent nonmedical usage has gone "underground," making it difficult to locate people who would admit to taking the drugs and producing sampling biases in subject selection (Blum, 1964).

Since much of the public furor over use of LSD was generated by claims that its use can engender permanent harm, it is important to investigate the evidence reporting ill effects to determine how closely its usage is related to long-term psychological damage. Reviews report adverse reactions to LSD (Greenblatt & Shader, 1970; Schwartz, 1968; Smart & Bateman, 1967), but attempts have not been made to differentiate between various conditions under which the drug was taken. In addition, these reviews failed to relate incidences in which follow-ups did not report ill effects.

The present study reviews the literature on long-term adverse psychological effects. Such a reaction is defined as pathological behavior (including suicide, psychosis, and severe anxiety) lasting for at least 48 hours after ingestion of the drug, the time by which the pharmacologic effects have usually subsided (Hoffer, 1965). These criteria for adverse reactions are difficult to follow in some cases since some reports did not distinguish between a dysphoric drug experience and a long-term effect. In addition, investigators have defined adverse reactions in different ways. In one survey (Ungerleider, Fisher, Goldsmith, Fuller, & Forgy, 1968), for example, a physician's biases toward LSD led him to state: "I would consider *all* reactions to LSD as 'adverse' regardless of the immediate subjective response [p. 355]." Reports of negative reactions which subsided with drug effects were not included. The bulk of the literature in this area consists of reports of adverse reactions, but in addition, studies which reported the use of LSD and included a follow-up of the users were included.

LSD has typically been administered under one of three basic conditions: (*a*) to psychiatric patients in research or psychotherapy programs; (*b*) in unsupervised, nonmedical settings, and (*c*) to normal subjects in research programs. Since the setting under which such drugs are taken influences the outcome of the experience, the present discussion is divided accordingly. Most of the literature consists of case studies and statistical surveys which could easily be criticized on methodological grounds. There are a few unusually clean and well-planned studies (Ditman, Tietz, Prince, Forgy, & Moss, 1967; McGlothlin, Cohen, & McGlothlin, 1967, 1968; Savage, Fadiman, Mogar, & Allen, 1966; Shagass & Bittle, 1967) but these are exceptional.

Psychiatric Patients in Psychotherapy and Research

Much of the original research with LSD was in drug therapy. Procedures and programs devised for LSD therapy have appeared (Abramson, 1967; Shlein, 1968, Section 3).

Cohen (1960) sent a questionnaire to 62 investigators using LSD or mescaline and received 44 responses with reference to nearly 5,000 individuals and more than 25,000 administrations. He reported four suicide attempts among patients (1.2 per 1,000 cases) and concluded that a direct connection between LSD and suicidal behavior could be discerned in very few instances. The one completed suicide, previously discussed by Savage (1957), was a chronic, regressed, schizophrenic girl with a 10-year hospitalization who had undergone LSD therapy. When inadvertently

allowed out of the hospital on a weekend pass, she committed suicide by throwing herself under a train.

Hoffer (1965), discussing Cohen's study, felt that the rate of suicide was very low considering the hopelessness of most of the patients and concluded that LSD may have decreased the rate since a high suicide rate could be expected in such a group. Smart and Bateman (1967), however, criticized Cohen's findings on the grounds that the rate of complications for the therapists who failed to respond may have been higher and that there was little follow-up of some of the patients. They reported 14 attempted and 6 successful suicides following Cohen's (1960) study, but concluded that it was difficult to attribute suicidal behavior to LSD since the cases were suicide-prone prior to drug use.

Malleson (1971) sent questionnaires to all physicians in the United Kingdom who were known to have used LSD on human subjects. Of the 74 physicians, 73 replied reporting on 4,300 patients with approximately 49,000 treatments, and 170 experimental subjects with 450 administrations. The reported suicide rate was .7 per 1,000 cases with three completed suicides and nine serious attempts. Eleven additional suicide attempts were reported, but no direct relation between the suicidal behavior and LSD ingestion could be determined. Response to this survey was nearly 100% and included approximately the same number of subjects but a larger number of administrations than Cohen's (1960) survey, thus speaking to the earlier criticism (Smart & Bateman, 1967) that the rate of complication was reduced due to the number of nonresponders.

Chandler and Hartman (1960) reported a case of suicide in a woman after her first treatment with LSD. She had a long history of alcoholism and narcotic addiction and had made three previous suicide attempts. Prior to the LSD session, she confessed to her therapist that she was planning to commit suicide on a particular night, and after an argument with her husband she made good her threat. This was the only adverse reaction in a project involving LSD therapy with 110 patients.

In Cohen's (1960) survey, eight instances (1.8 per 1,000 cases) of lasting psychotic episodes following LSD were reported, seven of these in patients undergoing therapy. Five had long-term courses while two went into remission within a few weeks. Malleson's (1971) survey reported 35 cases of psychosis (9 per 1,000), 19 of which recovered completely in less than 3 months. There were 10 cases of long-term psychosis, some of which were seen as potential psychotics who would have succumbed eventually regardless of LSD use. Details relating to the other eight psychotic episodes were unknown.

Cohen and Ditman (1962) reported five instances of psychotic breaks. They found underlying hysterical or paranoid personalities in each and concluded that the reactions were due to unskillful therapeutic management, permitting an upsurge of unconscious material which the patient was unable to handle. In a subsequent article (Cohen & Ditman, 1963) they reported several cases of prolonged psychotic decompensation, depressive reaction, and paranoid reaction in LSD therapy patients. In most of these cases psychological disturbances antedated the treatment, but the patients had been functioning outside a hospital. The authors concluded that the incidence of complications following LSD was probably infrequent, although unknown, and usually occurred in emotionally labile, hysterical, or paranoid personalities.

Fink, Simion, Haque, and Itil (1966) administered LSD to 65 psychotic subjects with an average hospitalization of 5.1 years. There were 158 administrations, and three prolonged reactions were noted, consisting of disturbances of mood, affect, and thought. The symptoms appeared to be an exaggeration of the patient's pretreatment state. The risk of negative reaction to LSD therapy was greater in subjects with emotional lability and psychotic features than in classical forms of schizophrenia.

In a follow-up of patients who underwent a single experience with LSD or mescaline, Savage, Savage, Fadiman, and Harman (1964) reported three negative incidents in questionnaire responses. One patient felt he did not receive enough support during the session and

suffered from obsessive ruminations for 9 months following the session, after which he improved. Another patient who had a long pre-LSD history of depression, hospitalization, and suicide attempts made another unsuccessful suicide attempt 2 months after the LSD session. A third patient did not keep his follow-up appointments and entered another facility where a second LSD treatment was proposed. He had a psychotic break on the evening of the proposed second session, but recovered. However, 83% of the respondents claimed lasting benefits, with an increase from 76% at 3 months to 85% after 6 months. The authors made clinical ratings on 74 of these patients 6 months after the session and found that 60 improved, 13 had not changed, while 1 was changed for the worse, although after 6 months of therapy he returned to his original base line. These ratings were based on clinical interviews and psychological data including the MMPI (pre- and post-) and the Leary Interpersonal Check List.

All of the preceding studies can be criticized on methodological grounds. A major flaw in each is the absence of a non-LSD control group comparable to LSD-taking patients in pretreatment pathology. One attempt to introduce experimental controls was made by McGlothlin and Arnold (1971) in a 10-year follow-up of 247 patients of three physicians who had experimented with LSD between 1955 and 1961. The experimental sample was matched with a control group of non-LSD patients from the same therapists based on psychological tests and attitude measures. No significant differences were found between the control group and subjects who had taken LSD only in therapist-initiated sessions. Of the experimental subjects, 19 were hospitalized with psychosis after their LSD experiences, but only one case was reported as being related to LSD ingestion. This was a patient who received three LSD treatments, was hospitalized 1 week after the final drug experience, and was unable to work for 3 months.

The above reports, although methodologically weak, indicate that the danger of psychiatric disturbance resulting from LSD is slight when the drug is used with proper subjects in well-supervised settings. Thus, the evidence does not provide grounds for discontinuing LSD treatment. Additionally, other projects did not report serious, prolonged, adverse reactions. Amarel and Cheek (1965) studied verbal behavior under LSD by administering 100 micrograms and 200 micrograms of LSD 1 week apart to 10 male alcoholic patients. They reported a 1-week follow-up after the second session with no adverse reactions. Bhattacharya (1966) reported on 581 LSD treatment cases and 2,742 administrations. He reported no cases of either temporary or permanent psychosis, no suicide attempts, and no behavior so bizarre that it was beyond control of the therapist.

Savage et al. (1966) reported on 77 patients who had psychedelic therapy over a 10-month period. Two thirds of the patients resembled typical psychiatric outpatient cases, while one third were mildly neurotic. The session consisted of a 200–300 microgram dose of LSD and lasted an entire day. The therapist was present to provide companionship but not interpretation. Patients were followed up to 6 months and were assessed by psychological tests, clinical evaluations, staff ratings, and behavior change. Results were generally positive and no adverse reactions were reported even though some patients were followed for up to 1 year.

Shagass and Bittle (1967) studied the effects of a large single dose of LSD 6 months and 1 year following the session. Patients were matched with non-LSD controls on sex, education, marital status, diagnosis, and symptoms. In addition, the experimental patients were divided into two groups: responders ($n = 8$), who displayed insight under LSD; and nonresponders ($n = 12$). Patients were rated on amount of improvement through an interview, and the experimental group improved significantly more than the control group ($p < .05$ at 6 months, $p < .02$ at 1 year). More controls than LSD subjects required follow-up therapy. No prolonged adverse reactions were reported.

Although it is apparent that LSD can produce an exacerbation of symptoms or psychotic behavior in some disturbed psychiatric patients, the literature is far from conclusive on the role of the drug experience in pathologi-

cal behavior. One of the major problems is the fact that base-rate statistics for suicidal behavior and psychosis among patients are not available. Sandison (1966) stated that both suicide and psychosis are possible complications of psychotherapy even when no drugs are used. Levine and Ludwig (1964) also felt the results support a conclusion that the drugs are safe and indicated that perhaps the incidence of negative reactions is just as high or higher for comparable patients in other active therapies. The result of several other reports (e.g., Buckman, 1968; Savage, 1968) in which LSD therapy produced positive results lends support to the contention that LSD can be a safe therapeutic instrument when properly administered to suitable subjects.

Reactions to Unsupervised Drug Usage

The majority of reported adverse reactions have been from instances where the drug was taken in unsupervised, nonmedical settings. Undoubtedly, most LSD ingestions have occurred under such conditions, but the exact number of administrations, purity, and dosage level remains unknown. The literature consists mostly of case reports and surveys rather than experimental studies.

Blumenfield and Glickman (1967) reported on 25 patients with a history of LSD use seen in the psychiatric emergency room of a hospital over a 10-month period. Thirteen were admitted with symptoms related to LSD and schizophrenic or "borderline schizophrenic" diagnoses. In addition, four suicide and two homicide attempts were noted. Seventy-two percent of the patients had psychiatric treatment prior to taking LSD, and 40% of these had psychiatric hospitalizations. The authors felt that the current hospitalizations were related to previous psychiatric difficulties and life situations rather than the effects of the drug. This conclusion was supported in a follow-up of 15 of these patients (Glickman & Blumenfield, 1967). It was found that the patients began LSD ingestion as an attempt to resolve a life crisis, and the stresses were the same types which often lead to hospitalization without drug use. The authors concluded not only that the psychoses and suicides would have occurred if the patients had not taken LSD, but the fantasy of "cure" through LSD may have helped to postpone the actual break.

A survey of negative side effects of LSD was reported by Ungerleider and his colleagues (Ungerleider, Fisher, & Fuller, 1966; Ungerleider, Fisher, Fuller, & Caldwell, 1968). Seventy patients whose diagnoses were related to LSD, seen over a 7-month period, were reviewed. Twenty-five of these were admitted to the hospital. Twenty-seven percent were diagnosed psychotic, 21% neurotic, and 18% character disorder. Ten percent had previous psychiatric hospitalizations and 27% had received psychiatric outpatient care. The 25 inpatients were compared with a "control" group of 25 frequent LSD users, a group of rehabilitated criminals, who were not hospitalized to determine correlates of adverse reactions. The groups were compared on demographic background, marital status, employment, police record, education, previous psychiatric care, and the MMPI. Significant differences were found for marital status (0% inpatients married versus 60% controls, $p < .001$), employment (20% inpatients working versus 70% controls, $p < .01$), and police records (8% inpatients versus 64% controls, $p < .001$). This latter finding was due to the fact that the control group was composed of rehabilitated criminals. The inpatient group displayed severe psychopathy on the MMPI, but similar findings were not present in the controls.

Ditman et al. (1967) were also interested in why some people had adverse reactions while others did not and may even have found LSD therapeutic. Subjects were 116 people who had taken LSD. Group 1 ($n = 52$) consisted of people who did not need psychiatric care. Most were students or working people. Group 2 ($n = 27$) consisted of psychiatric outpatients who applied for treatment as a result of LSD ingestion, and Group 3 ($n = 37$) was composed of psychiatric patients hospitalized because of LSD use. Groups were compared on the basis of an interview, demographic variables, drug history, and the DWM Card Sort Test, an instrument developed to assess LSD experiences. The employment status of subjects was assessed prior to hospitalization but after they had taken LSD. The per-

centage of subjects who were employed or were full-time students was significantly higher in Group 1 than in Group 3 ($p < .001$). Since this was not assessed until after the subjects had taken LSD, however, a cause–effect relation cannot be determined. On the DWM Card Sort Groups 2 and 3 reported more unpleasant feelings under LSD than Group 1 ($p < .01$) and more intense feelings of despair and hopelessness ($p < .05$). Items reflecting a a positive, beneficial experience were reported more frequently by Group 1. The authors concluded that unstable individuals who take LSD without support and protection are likely to find the experience disruptive, while the results in the nontreatment group supports the notion that LSD has a potential value for research in psychotherapy and esthetic appreciation.

Frosch, Robbins, and Stern (1965) studied 12 of 27 patients admitted to a hospital as a result of LSD ingestion over a 4-month period. Seven were diagnosed as panic reactions, three had a reappearance of the drug symptoms without reingestion of the drug, and three were psychotic. The panic reactions rarely led to hospitalization. Of the three with reappearing symptoms, two were diagnosed as chronic schizophrenics and the other was a borderline psychotic. The three with extended psychoses following LSD ingestion had clear long-standing schizophrenia: two were catatonic and one was paranoid. The schizophrenic patients developed a unique sense of "insight" under LSD and were subsequently unable to adapt to the environment. A second sample ($n = 22$) was taken from the same hospital and compared with the original group (Robbins, Frosch, & Stern, 1967). This group had more drug experiences but the symptoms still fell into the same three categories: (*a*) 11 panic reactions, (*b*) 8 symptom reappearances, and (*c*) 8 extended psychoses. The recurring symptoms were seen in repeating users when exposed to an anxiety-arousing situation and were felt to involve psychological as well as physiological factors. Contrary to earlier findings, three of the psychotics were seen as not psychotic before taking LSD, although suggestions of severe personality disturbance were present. The authors warned that adverse effects could not always be predicted from previous history.

Louria (1967) reported over 130 patients hospitalized with LSD-induced acute psychoses, or chronic schizophrenia, and schizoid personality exacerbated by LSD. Of these, 34.2% were reported as having underlying personality disturbance, and the author concluded that an increasing number of susceptible, unstable individuals were being influenced to use LSD.

Not all studies have indicated preexisting psychiatric difficulties in those becoming psychotic. Tietz (1967) reported a study of 49 patients admitted to an inpatient service with LSD-related complications. Eighty percent were from the lower socioeconomic class, and dosages from 100 to 2,000 micrograms were reported. Patients received psychological testing and had Bender-Gestalt tests within normal limits, but MMPI profiles similar to schizophrenics. Fifteen had acute panic reactions, 5 requiring hospital care, while 6 had recurring symptoms and 28 had extended psychoses. Conclusions are limited by the lack of information on premorbid adjustment, but none had previous psychiatric hospitalizations.

Many reports on LSD reactions have been case studies, which, although valuable for gathering data, fail to provide a basis for determining a relation between LSD and subsequent reactions since they lack experimental controls. Appropriate caution must be used in making conclusions from these studies.

Bowers, Chipman, Schwartz, and Dann (1967) reported three cases of adverse reactions to LSD, two requiring treatment. A 19-year-old college sophomore was admitted with depression and disorganization after having taken LSD. The history revealed a poor childhood, a previous long-term hospitalization, and an inability to relate to others. A 20-year-old medical student was seen as an outpatient for five sessions because of anxiety following LSD but was not considered seriously disturbed. The authors concluded that each patient had intense needs for interpersonal closeness and no access to meaningful emotional experiences. Muller (1971) reported three cases of prolonged LSD effects leading to hospitalization. All were released after 2

weeks, although two returned after a short period with a relapse of symptoms. Electroconvulsive treatments produced remission in these cases.

Two cases of psychosis due to LSD ingestion of sufficient severity to warrant hospital admission were reported by Hatrick and Dewhurst (1970). Only one dosage of LSD was involved in each case, and in one case it was administered to the patient surreptitiously. Both patients had well-adjusted premorbid personalities, no previous history of regular drug use, and both appeared normal for between 2 weeks and 2 months before the onset of psychotic effects. Although the symptoms abated within a number of weeks, the authors concluded that these cases were of sufficient severity to warrant the removal of LSD from use in psychotherapy. In a rebuttal, Malleson (1970) argued that the nature of the relation between the drug and illness was indeterminable, the pathology was more likely brought on by emotional upset in the patients, and the conclusion that such therapy should be discontinued was not justified on the basis of anecdotal information.

Efforts to determine the relation between LSD and psychiatric disturbance have also been weakened by unreliable and subjective psychiatric diagnoses. Often, reports appear to be based on value judgments, and patient attitudes and life-styles rather than standard diagnostic criteria. Rossi (1971) discussed the "psychedelic syndrome" as one form of adverse reaction characterized by preoccupation with mystical subjects, belief in astrology and extrasensory perception, and a rejection of societal values. He related LSD usage in such cases as an attempt to avoid the decision between social commitment and passivity. Glass and Bowers (1970) reported four LSD-related cases hospitalized by their families because of bizarre behavior, appearance, and withdrawn manner. The patients had mystical attitudes, belief in oriental religions, and perceived themselves as passive agents manipulated by cosmic forces. All were well oriented with a good memory for recent events, although recall of past events was vague, and visual hallucinations and paranoid delusions were present. In each case, heavy drug use and subsequent reactions appeared when the patients were facing heavy stress. The authors inferred that heavy drug use may have affected concurrently developing attitudes and values, thus facilitating the acquisition of mystical beliefs. A major difficulty with this interpretation is the fact that mystical beliefs are shared by a large number of young persons with no history of LSD use. It is equally possible that the adverse reactions were due simply to an inability to deal with stress situations. The diagnosis of unpopular attitudes and mystical beliefs as psychiatric symptoms is based on cultural value judgments rather than objective psychiatric criteria and only obfuscates understanding of drug effects.

Although it is evident that persons may develop serious psychological disturbances after taking LSD, a causal relation between the two events is most difficult to determine. In nearly every case where a prolonged reaction was noted, the history showed signs of psychological disturbances which antedated drug use. In addition, evidence indicates that many persons who take the drugs do so with a belief that it will help them solve their emotional problems. It is impossible to determine the number of unsupervised LSD ingestions, but even with the most conservative estimates it is obvious that many more persons are using the drug than are having negative effects. The most reasonable conclusion from the preceding section is that LSD can cause psychological difficulties in disorganized and disturbed individuals who ingest the drug in less than secure surroundings, without psychological support, and at a time when emotional problems or crises are at a peak.

Use with Experimental Subjects

Although many experiments studying the effects of LSD on normal subjects have been reported, most investigated the effects of acute intoxication on psychomotor or psychological tasks. Few of these studies followed the subject for any period of time after the drug experience. As a result, although many reports appear, few are relevant to the present review. Studies investigating LSD and including a follow-up are discussed first, followed by studies designed to explore long-term effects.

Abramson and his colleagues performed a long series of experiments assessing the effects of LSD on many psychological and physiological responses (e.g., Abramson, Jarvik, & Hirsch, 1955; Abramson, Jarvik, Kaufman, Kornetsky, Levine, & Wagner, 1955). They used many of the same subjects in over 150 experiments over a 10-year period. The records of six subjects were shown (Abramson & Rolo, 1965) and no adverse reactions were reported. The possibility of adverse reactions was discussed and it was felt that no danger existed as long as drug usage was supervised by a physician.

In an experiment comparing the LSD experience to schizophrenia, Langs and Barr (1968) gave LSD to 30 normal subjects. Eight subjects with anxious, manipulative, and hostile traits on predrug testing showed behavior similar to paranoid schizophrenics while under LSD, but no long-term adverse effects were found. In two studies involving 69 penitentiary inmates, Katz, Waskow, and Olsson (1968) gave 50 micrograms of LSD to 23 subjects and found either euphoric, dysphoric, or ambivalent responses. No adverse reactions were reported. Keeler (1965) gave psilocybin to 12 normal subjects, personnel at the research center where he worked, and found significantly higher scores on the schizophrenia and hypochondria scales of the MMPI from the pretest to a test taken while under the drug. Since the subjects had employment contact with the experimenter after the session, a long follow-up is assumed, but no adverse reactions were reported.

Welpton (1968) performed an intensive week-long study of LSD users and gave them LSD under his supervision. Extensive screening, testing, and interviewing were undertaken and poor family histories as well as some psychological maladjustment were found. "The most impressive finding was the relative infrequency of adverse reactions to LSD and other hallucinogens considering the degree of personality disturbances [p. 378]." In Cohen's (1960) original survey, one psychotic reaction in an experimental subject was reported. This was a man who was an identical twin of a hospitalized schizophrenic, and the reaction subsided within a few days. Pollard and Uhr (1965) reported on 5 years of experimentation using LSD and psilocybin with 80 college student subjects and reported no persistent ill effects, due to careful subject screening.

The low incidence of negative experiences among experimental subjects is even more impressive considering a series of findings reported by Cohen (1960). He related several studies in which the following reactions were attributed to the drug experience: migraine headaches, influenza, paraplegia, a suicide attempt, and a skin rash. All of these reactions occurred in control subjects who received water placebos. This finding indicates that hysterical, suggestible subjects may explain subsequent difficulties on the "drug" experience, indicating that reactions reported due to the drug may have been related instead to personality factors.

One of the most extensive and well-controlled programs to investigate the long-term effects of LSD was conducted by McGlothlin et al. (1967, 1968), assessing change due to LSD in personality, attitudes, values, interests, and performance among normals. Subjects ($n = 72$) were male graduate students who volunteered for the experiment without knowing it involved LSD. Their knowledge of LSD was determined and those with LSD experience, currently in psychotherapy, or psychoses in the family were screened out. Others were dropped because of interview impressions or doubtful MMPI profiles. Subjects were given a battery of tests assessing anxiety, personality, attitudes, esthetic sensitivity, and creativity. Then, they were divided into three groups of 24, matched with respect to knowledge of the drugs and expectations, and received the following drugs in a double-blind design: Experimentals, 200 micrograms of LSD; Control 1, 20 milligrams of amphetamine; and Control 2, 25 micrograms of LSD (below threshold dosage). Subjects met for three sessions and received the same drug and dosage each time. On 2-week and 6-month follow-ups, subjects were retested with the same instruments. Thirty-three percent of the experimental subjects had lower anxiety scores compared to 13% in Control 2 and 9% in Control 1 after 2 weeks. Experimental subjects had a significantly lower galvanic skin

response to stress at the 6-month follow-up. Sixty-two percent of the experimental subjects reported an increased appreciation of music, which was supported by behavioral changes such as buying records and attending concerts. Other tests showed differences in favor of the experimental group but most failed to reach statistical significance. No adverse reactions were reported, although one subject was terminated due to an "unrealistic reaction" to the first drug dose.

Ditman, Hayman, and Whittlesey (1962) studied 74 subjects with LSD experiences from 6 months to 3½ years prior to the follow-up. Half the subjects were "normals" and half were psychiatric patients, and each received 100 micrograms of LSD. Questionnaires regarding the experience were completed at the follow-up and 66% reported some degree of benefit. Patients claimed more improvement than normals, although normals reported more pleasant LSD experiences. The authors concluded that if subjects' claims are valid, the LSD experience may be therapeutic in itself. No adverse reactions were reported.

An investigation of the effects of LSD on problem solving and creative abilities was reported by Harman, McKim, Mogar, Fadiman, and Stolaroff (1966). Subjects were 27 male professionals whose work required creative problem-solving abilities (engineers, physicists, mathematicians, architects, artists). They were found to be psychiatrically normal and motivated to discover and apply problem solutions within their professional capacity. They were asked to select a problem and encouraged to work on the problem under the drug. Subjects were given 200 micrograms of mescaline sulfate (equal to 100 micrograms of LSD) in groups of four, accompanied by two observers. They relaxed and listened to music for 3 hours, spent 1 hour on psychological testing, and worked on their problems for 3–4 hours. The psychometric data reported significant increases in creativity while under the drug and at the 2-week follow-up subjects reported significant changes in their functioning which related to their enhanced abilities during the drug experience. Subjects were seen 6 weeks after the session and no adverse reactions were reported.

The above studies indicate quite clearly that when psychologically well-adjusted individuals took LSD under controlled, secure, environmental situations where support was available, no long-term adverse reactions occurred.

Conclusions

The major conclusion of this review is that research on LSD, particularly its long-term psychological effects, is very poor. Most studies are based on subjective case reports, surveys, or used very weak experimental controls. The lack of comparable control groups and base-rate statistics for nondrug therapies makes interpretation of studies with patients very difficult. Any direct relation between drug use and subsequent behavior remains strictly conjectural. In many case studies, interpretations of behavior were often based on the biased judgment of the investigator rather than any standard criterion. Very few controlled studies investigating the areas of psychological functioning affected by LSD, especially those areas espoused by proponents of consciousness-expanding experiences, have appeared. The work of McGlothlin et al. (1967, 1968) represents the type of research with the greatest potential for generating scientific knowledge of the drug's effects.

Those adverse reactions which have occurred were most frequent among individuals who were emotionally disturbed, in crisis situations or insecure environments, and who took the drug in unsupervised settings. Psychotic episodes and suicidal behavior, while rare, have occurred in such circumstances. The few well-controlled studies indicate, however, that when the drug was administered to psychologically normal subjects under secure circumstances, lasting adverse reactions did not occur. Thus, the concerns which led to discontinuation of research are unsubstantiated, and the type of controlled research discussed above could be resumed without undue danger to subjects.

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