LSD Psychosis or LSD-Induced Schizophrenia?

A Multimethod Inquiry

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• **We studied whether patients hospitalized for LSD psychosis are clinically separable from acute schizophrenics. The family histories, manifest symptoms, premorbid adjustment, and profiles on an extensive test battery were analyzed for 52 LSD psychotics and 29 matched first-break schizophrenics. The LSD patients did not differ from schizophrenics in incidence of psychosis or suicide among the parents. However, the rate of parental alcoholism for LSD psychotics far exceeded that for schizophrenics and the general population. The two groups were distinguished on some clinical features but were equivalent in premorbid adjustment, on most cognitive measures when initially hospitalized or reassessed three to five years later, and in number of subsequent rehospitalizations. Thus, in most respects the LSD psychotics were fundamentally similar to schizophrenics in genealogy, phenomenology, and course of illness. The findings supported a model of LSD psychosis as a drug-induced schizophreniform reaction in persons vulnerable to both substance abuse and psychosis.**
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One of the key issues related to the adverse effects of LSD is whether the occasional prolonged psychotic sequel constitutes a distinct syndrome or, rather, a non–drug-specific reaction in personalities vulnerable to stress. The first model corresponds to that of toxic psychosis, whereas the second views LSD as a precipitant of schizophrenia among those so predisposed.[1]

Early studies focused mainly on individual differences in susceptibility to the immediate, temporary psychoticlike reaction to LSD. For example, Klee and Weintraub[2] reported that persons who were mistrustful, complaining, fearful, and reliant on projection as a defense were more likely to have paranoid symptoms during the LSD experience. In a study of normal subjects given LSD experimentally, Langs and Barr[3] observed that psychoticlike experiences were anticipated by predrug Rorschach indicators of paranoid features and potential for thought disorder. Of particular interest is the finding of drug-induced psychotic symptoms in 18 of 20 relatives of schizophrenics,[4] suggesting that persons with greater genetic predisposition to schizophrenia are more susceptible to a psychotic response.

The question of a distinct LSD-induced psychotic syndrome was confronted more directly by a group of studies that examined the antecedents of prolonged psychotic decompensation following use of the substance. This is the relatively enduring clinical condition commonly referred to as LSD psychosis, which resembles acute schizophrenic reaction and persists well after the 24-hour period that the drug action usually takes to run its complete course.[1,5-8] The clinical and retrospective studies of these prolonged psychotic reactions suggest that adaptive problems may have existed prior to the drug-related psychotic symptoms. Some authors, for example, have proposed that the LSD casualties comprised a group who had already been chronic schizophrenics[9] or victims of personal crises that antedated LSD ingestion.[10] Unfortunately, such reports in the main were derived from descriptive case studies or research that lacked sound experimental design and controls.[6,9,10]

Hensala and his colleagues[11] made the first attempt at a small-scale controlled study of LSD casualties. Comparing 20 hospitalized LSD psychotics with other psychiatric inpatients, they investigated a number of premorbid psychosocial variables, including family reports, personal histories, and work experience. They concluded that the LSD group had had a poorer occupational adjustment, more atypical sexual adjustment, and a greater number of "antisocial premorbid personalities." In examining the psychiatric histories of the parents in both groups, they found no significant difference in rate of "overt mental illness" but a fairly high (15%) rate of alcoholism in the parents of LSD psychotics. More recent studies of family loadings similarly found no measurable differences between psychotic inpatients with prior drug involvement and acute psychotic[12,13] or schizophrenic controls.[14] In contrast to the observation of Hensala et al, the premorbid adjustment of these drug-related groups, as rated on the Phillips or Stephens-Astrup Scale, was found to have been better than that of the schizophrenic comparison groups.[12,14] Accordingly, Breakey

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et al suggested, "On the basis of these results it seems plausible to conclude that the taking of drugs . . . might play some precipitating role in the onset of schizophrenia, bringing this disorder on more quickly."[14(p260)] Confidence in this summation, however, must be tempered by methodologic limitations in the latter group of studies. These include small and unbalanced samples,[12-14] vague and nonobjective criteria for some of the dependent variables,[11-13] and an index group that included patients who had never used LSD[12-14] or were already identified as schizophrenics and without specific drug precipitation.[14]

In regard to objective assessment, there is a paucity of psychological test data with hospitalized LSD casualties, and no published reports of which we are aware involving a battery of more than two standardized tests. In one study, Ungerleider et al[15] gave the Minnesota Multiphasic Personality Inventory (MMPI) to 27 LSD inpatients and 25 LSD users who had no decompensation. They found the "schizophrenia" scale to be highest among the LSD users who had prolonged psychosis and concluded that "LSD interacts with schizoid traits," although not presenting sufficient evidence that such trends antedate the decompensation. In another MMPI study, Smart and Jones[16] detected higher incidence of signs reflecting conduct disorder and psychosis in nonpsychotic LSD users as compared with normal controls. Finally, a study by Tucker and associates[17] compared hospitalized LSD and other hallucinogenic-drug casualties with schizophrenic inpatients on Rorschach scales of thought disorder. They found the drug group higher than schizophrenics on associative productivity, intrusion of primitive drive content, and penetration scores. Thus, the LSD-related psychotics were regarded as showing more, rather than less, defense inadequacy than schizophrenics.

The foregoing studies, in sum, appear to suggest that premorbidly the LSD psychotic has an antisocial personality with schizoid traits and a genealogic predisposition to substance abuse and schizophrenia (cf review by Stone[8]). This view supports a model whereby the toxic effects of LSD interact with premorbid schizophrenic vulnerability to produce a sustained psychotic reaction. The literature to date, however, provides inadequate data base and objective measurement to substantiate conclusions about susceptibility to psychosis, premorbid adjustment, symptom profile, cognitive impairment, and long-term clinical course of these LSD-linked casualties. The present work was therefore aimed at these multiple aspects of the condition with the purpose of examining the issue of whether LSD psychosis is distinguishable from non–drug-related acute schizophrenia.

First, we investigated the nature and incidence of parental illness among the LSD psychotics. Our assumption was that, if the character and frequency of parental illness are comparable with what is seen in schizophrenia and contrasting to the general population, this would be evidence of premorbid susceptibility to the development of a prolonged psychotic reaction.

Second, to obtain multidimensional assessment of clinical features, premorbid adjustment, and cognitive functioning, we compared LSD psychotics and acute schizophrenics on manifest symptoms, the Phillips Scale, psychologists' written evaluations, and a battery of objective tests measuring intellectual profile, organicity, and thought disorder.

Third, because the fate of LSD psychotics after the acute phase has not (to our knowledge) been systematically investigated, we followed up these patients and a comparison group for a period of three to five years. We investigated residual abnormality in terms of incidence of relapse and results of subsequent testing.

SUBJECTS AND METHODS

The participants in this study were selected from 110 first-admission inpatients who, between 1967 and 1972, had been hospitalized for treatment in the training unit of a large urban psychiatric center. Of these, 52 were classified as having LSD psychosis, based on reports of psychotic symptoms (hallucinations, delusions, thought disorder) that first appeared and persisted at least two weeks after LSD ingestion. Frequency of LSD intake was most commonly one to five times (in 18 [34.6%] of the cases), occasionally six to ten times (7.7%), but ranged up to about 100 times, as reported by two subjects. Although these patients often acknowledged more general drug experience, in all cases the psychosis reportedly developed following the use of LSD alone.

On admission, mental status examinations and diagnoses were rendered conjointly, and independently of the current project, by a supervising psychiatrist and psychiatric resident, following an interdisciplinary case conference. These indicated a clinical picture comparable with that described for LSD casualties in Stone's review.[8] The prevalent symptoms consisted of impaired affect (in 26 [50.0%] of the cases), hallucinations (24 subjects [46.2%]) that were mainly of auditory (12 subjects [23.1%]) and visual (11 subjects [21.2%]) nature, delusions (16 subjects [30.8%]) with about equal frequency of persecutory, grandiose, somatic, and guilt content, depression (18 subjects [34.6%]), suicidal ideas or actions (17 subjects [32.7%]), schizoid features (15 subjects [28.8%]), antisocial behavior (14 subjects [26.9%]), and thought disorder (13 subjects [25.0%]). In terms of diagnosis, which conformed to the *DSM-II* nosology and criteria, 37 cases (71.2%) were classified as schizophrenic, including 15 (28.8%) of paranoid subtype, and 16 (30.8%) were considered also to have incurred some form of personality disorder, most often antisocial personality (5 cases [9.6%]).

From this pool of 52 LSD patients, a subgroup of 29 cooperated in undergoing a battery of psychological tests. The procedures were administered between ten and 14 days after transfer to this hospital, and three to four weeks following admission to their initial hospital. This lapse in time allowed for dissipation of the direct toxic effects of LSD, adjustment to the hospital milieu, and preliminary response to neuroleptic drugs. Thus, patients were tested in the early phase of treatment, after the most active manifestations of psychosis had generally subsided.

A comparison group consisted of 29 first-break schizophrenics, who were drawn from the same unit and agreed to the testing program. They were tested also approximately two weeks after arrival on the unit (three to four weeks after initial hospitalization). This group was equivalent to the index group in age at hospitalization, education, and major demographic features. Patients with LSD experience, any record of drug abuse, prior hospitalization, mental retardation, or questionable diagnostic classification were excluded from this sample. Those with a schizoaffective diagnosis were also excluded to guard against possible selection of patients with an affective syndrome. A schizophrenic diagnosis was established for all 29 patients by consensus between a senior psychiatrist and two psychologists using *DSM-II* criteria. Of this group, 17.6% were classified as paranoid subtype. In applying the more recent *DSM-III* classification, a retrospective analysis of the case records confirmed that all fulfilled the criteria for schizophreniform disorder (ie, schizophrenia of less than six months' duration). Their predominant symptoms, as reported in the admitting mental status examinations, consisted of delusions (in 20 subjects [70.6%]), mainly of persecutory type (12 subjects [41.2%]), hallucinations (19 subjects [64.7%]), thought disorder (14 subjects [47.1%]), and impaired affect (14 subjects [47.1%]). The symptom of depression was observed in only three cases (11.8%).

From the groups of 29 LSD psychotics and 29 first-break schizophrenics who underwent the full inpatient evaluations, 21 in each sample (72.4%) could be reassessed three to five years later (mean, 3.52 years for the LSD group and 3.81 years for the comparison group). Patients at this time were contacted by letter and, where possible, by telephone as well, and they were offered payment for their participation in the follow-up. The testing was performed in the hospital's outpatient clinic except for two cases, in which it was necessary to make home visits to obtain the data. Whereas all patients had been receiving neuroleptics when initially tested during their hospitalization, only 13 from the LSD group and

Table 1.—Sample Characteristics

Characteristic	LSD Psychotics: Full Sample (n=52)	LSD Psychotics: Final Sample (n=21)	Acute Schizophrenics (n=21)
Age, yr			
Mean	20.46	19.81	20.71
SD	4.97	3.09	4.21
Range	14-39	14-27	15-33
Education, yr	12.11	13.05	13.43
Sex			
M	39	17	8
F	13	4	13
Ethnic group			
White	40	17	15
Black	6	2	4
Hispanic	6	2	2
Religion			
Jewish	21	10	8
Catholic	20	6	8
Protestant	11	5	5
Marital status			
Never married	45	16	17
Married	4	2	3
Separated/divorced	2	3	1
Widowed	1	0	0

12 from the comparison group were still taking controlled medication at the time of follow-up. Of those from the LSD sample who could not be reassessed, three subjects could not be located, four refused to cooperate, and one had committed suicide. In the comparison group, there were two unlocatable subjects, five refusers, and one suicide. The outcomes of these lost cases, hence the representativeness of the remaining subjects, could not be determined.

Table 1 gives the sample characteristics for the LSD psychotics and 21 patients from the LSD and comparison groups who received the two testings and thus were included in the final analyses. The demographic profiles suggest that both groups were composed of primarily middle class subjects. It can be further seen that the LSD and comparison samples were highly similar on all dimensions except sex. The schizophrenic group was slightly overrepresented by women whereas the LSD casualties, in keeping with epidemiologic surveys,[18] were strongly dominated by men.

Procedures

The following avenues of inquiry were pursued.

Case Histories.—The incidence of psychiatric illness in the parents of the 52 LSD subjects was obtained from review of their extensive case histories. These had been prepared by the unit's psychiatric residents in concert with their supervisor after interviews with the patients and their families. Based on these semistructured documents, the following categories of illness in the parents were identified: psychosis, where the records indicated hospitalization for schizophrenia, major affective disorder, or "mental illness"; suicide, where such was reported; and alcoholism, where a history of alcoholism or heavy drinking was specified. Considering the probable bias of families against acknowledging mental disorders as well as the ever-present possibility of errors of omission, the data thus obtained are considered *minimal* estimates of parental illness.

Symptom Checklists.—To enable a broad-based comparison of clinical features, the reports of various manifestations of disease in patients' official case records were systematically notated on symptom checklists. The detailed mental status reports, confirmed by a supervising psychiatrist, were independently reviewed by two psychologists for presence or absence of each of 66 symptoms that constituted 15 symptom categories, such as delusions, thought disorder, hallucinations, and impaired affect. The degree of concordance between these two raters was significant for all categories ($P<.001$), with a mean ϕ coefficient of .84. In the same way, the prevalence of an additional 14 qualitative features (identified in Table 2) was studied by review of patients' psychodiagnostic test reports. These had been written according to a structured format by psychology interns, under direct supervision of a senior psychologist, after administration of standard intellectual and projective measures.

Table 2.—Comparison of Pathologic Features Reported in Psychological Test Evaluations

Trait	χ^2	P	Group With Greater Frequency
Passivity	4.02	<.05	LSD psychotic
Evidence of chronicity	2.93	<.10	LSD psychotic
Sense of impairment	11.77	<.001	Schizophrenic
Confusion and/or disorientation	5.37	<.05	Schizophrenic
Clinging dependency needs	4.37	<.05	Schizophrenic
Concern about illness/impairment	3.70	<.10	Schizophrenic
Bland affect	2.69	NS	. . .
Controlled by external forces	1.90	NS	. . .
Lack of insight into illness	1.73	NS	. . .
Depersonalization/derealization	1.37	NS	. . .
Blurred self-other discrimination	1.14	NS	. . .
Symbiotic and/or fusion needs	0.13	NS	. . .
Suggestive of organicity	0.01	NS	. . .
Evidence of organicity	0.01	NS	. . .

Premorbid Adjustment.—The premorbid adjustment of patients was assessed using the Phillips Scale, part I,[19] which correlates strongly with the rest of the scale ($r=.98$).[20] The main sources for this evaluation were the detailed case histories and personal interviews with the patient.

Psychological Testing.—A battery of objective tests was applied to obtain standardized measurement of deficits in the cognitive sphere. Subtest scatter on the Wechsler Adult Intelligence Scale (WAIS) was used for assessing the intellectual profile and cognitive integrity of subjects. The test was selected for its well-established norms and its sensitivity to deficits in the clinical population[21] as well as to impairments under LSD in normal subjects.[22] Also for longitudinal use, this measure has been found to reflect changes in the clinical course of schizophrenic patients, indicating either improvements or chronicity of illness.[23]

Visual-motor disturbances, as possible indication of organic influence, were studied with two widely used neurologic screening procedures. The Bender-Gestalt Test, involving reproduction of simple designs by copy, was scored according to the Pascal-Suttell[24] criteria for reproduction errors. This system penalizes the examinee for failures in maintaining orientation, proportion, and an integrated configuration. The Benton visual retention test is similar in principle to the Bender-Gestalt but also requires perceptual recall. It was scored for the number of correct designs and number of errors.[25]

The Rorschach test was included in the battery because it has been found sensitive to personality changes induced by LSD experiments[26] and to cognitive disorders in LSD psychotics.[17] In contrast to some previous studies that applied the traditional scoring categories of the Rorschach, we confined ourselves to only those objective scales that have clearly differentiated psychotic from nonpsychotic patients. Using blind raters, the test protocols were scored for two cognitive dimensions that have yielded good interrater reliability: (1) Becker's Developmental Level (DL)[27]; this scoring system proceeds from the concept of distinguishing between differentiated and undifferentiated percepts as an index of developmental maturity. As such it applies Werner's developmental theory and approaches schizophrenic disorder from the standpoint of regression to an earlier functional level. (2) Thought

Table 3.—Incidence (%) of Psychosis, Suicide, and Alcoholism in Parents of LSD Psychotics Compared With Other Groups*

Parental Illness	LSD Psychotics	Comparison Group† Schizophrenics	Comparison Group† General Population
Psychosis			
Mother	7.7	8.1	1.4‡
Father	5.8	4.6	1.3§
Either parent	13.5	12.7	2.7‡
Suicide			
Mother	3.8	1.4	0.4‡
Father	3.8	4.2	1.6
Either parent	7.7	5.6	2.0‖
Alcoholism			
Mother	7.7	0.8‡	0.5†
Father	23.1	12.3§	4.0‡
Either parent	30.8	13.1‖	4.5‡

*Results are of χ^2 analysis with 1 *df*.

†Data pertaining to psychosis and alcoholism in the parents of 260 schizophrenics are based on Fowler et al[31]; data on suicide among the parents of 73 schizophrenics are based on Stephens et al.[33] For general population, incidence for psychosis is based on prevalence of schizophrenia and manic-depressive illness, according to Freedman et al[32]; for suicide, based on the World Health Organization[34]; and for alcoholism, based on Goodwin.[35]

‡$P<.001$.

§$P<.05$.

‖$P<.005$.

Table 4.—Comparison of LSD Psychotics and Acute Schizophrenics on Premorbid Adjustment, Intelligence, Visual-Motor Deficits, and Rorschach Scales

Assessment Procedures	LSD Psychotics, Mean	(SD)	Acute Schizophrenics, Mean	(SD)	*t*
Phillips Scale	13.52	(4.65)	13.38	(5.00)	0.09
Wechsler Adult Intelligence Scale					
Full-scale	107.29	(13.40)	101.29	(13.03)	1.47
Verbal	112.43	(13.81)	107.52	(13.08)	1.18
Performance	99.71	(12.54)	93.67	(14.61)	1.44
Bender-Gestalt Test	79.13	(24.96)	79.50	(18.11)	0.05
Benton Test					
No. correct	6.67	(1.56)	6.62	(1.53)	0.10
No. errors	5.67	(3.20)	5.33	(2.48)	0.38
Rorschach scales†					
R	22.26	(9.86)	20.26	(7.09)	0.72
TQ, %	18.95	(18.74)	7.42	(9.70)	2.38*
AE, %	4.32	(6.74)	2.79	(3.26)	0.89
OS, %	20.53	(21.34)	13.84	(15.99)	1.09

*$P<.05$.

†R indicates response number; TQ, thought quality; AE, affect elaboration; OS, overspecificity.

disorder; to evaluate the nature and severity of thinking disturbance, we adopted the scoring system of Quinlan et al,[28] which distinguishes reliably between psychotic and nonpsychotic populations. Derived from the works of Rapaport et al[29] and Watkins and Stauffacher,[30] this method scores for three different manifestations of deviant thought processes: thought quality (TQ), which assesses the extent of arbitrariness in logic and reasoning and the peculiarity of verbalizations; affect elaboration, reflecting degrees of affective qualities projected onto the inkblots; and overspecificity, which evaluates tangential thinking and looseness of associations as manifested by the relatedness of responses to the stimulus characteristics of the card. These indexes were expressed as the ratio of clearly deviant responses (a scaled score of 2 or greater) out of the total number of Rorschach responses. In this way the borderline or questionable instances of disordered thinking were eliminated and there was adjustment for productivity, which is known to correlate significantly with these scales.[17]

RESULTS

Manifest Symptoms

Analysis of symptoms reported in the mental status examinations early during the course of hospitalization unveiled some differences in the clinical picture of LSD psychotics compared with first-break schizophrenics. The LSD patients showed significantly less occurrence of delusions than the comparison group (30.8% *v* 70.6%, $P<.005$, χ^2 test). There were also fewer LSD psychotics with overt thought disorder (25.0% *v* 47.1%) and more with depressive traits (34.6% *v* 11.8%), although these differences only approached significance ($.10>P>.05$). The remaining 12 symptom categories did not significantly differentiate these groups.

Parental Illness

Table 3 gives the incidence of psychosis, suicide, and alcoholism in the parents of LSD psychotics as compared with the rates for parents of schizophrenics and the general population. It was found that for the LSD group, the incidence of parental psychosis requiring hospitalization (13.5%) was slightly above that obtained for a schizophrenic population (12.7%) in a recent large-scale study that used similar methods and criteria.[31] In contrast to the lack of significant differences between these groups, the LSD psychotics showed significantly higher rates of hospitalization for psychosis among both mothers and fathers as compared with the general expectancy rates.[32]

In a similar vein, the incidence of suicide among the parents of LSD psychotics (7.7%) was somewhat higher than the parental suicide rates observed with schizophrenics (5.6%) by Stephens et al,[33] though not significantly so, but was significantly beyond the rates obtained in the general population.[34] Of special interest was the prevalence of heavy drinking or alcoholism in the mothers and fathers of the LSD patients (30.8%). These rates significantly exceeded those for parents of schizophrenics (13.1%)[31] and the general population (4.5%)[35] but were comparable with the rates noted among parents of alcoholics (25.0%).[36]

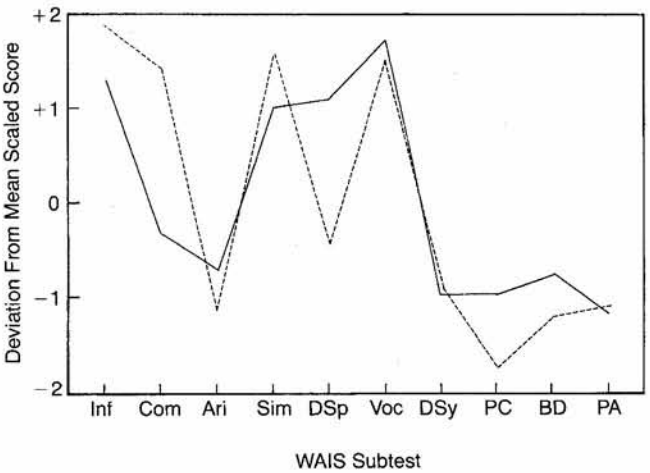
Premorbid Adjustment

Group comparison of premorbid social and sexual adjustment on the Phillips Scale (Table 4) revealed no significant difference. Using the customary criterion of 15 points or higher as the index of poor premorbid record, both groups were found to include a sizable proportion of "bad premorbids": 38.1% among the LSD psychotics and 42.8% among schizophrenics.

Cognitive Test Impairment

Intellectual Profile.—The scores on the WAIS, based on ten subtests, were compared for the 21 LSD psychotics and 21 schizophrenic patients. Two types of analyses were conducted with these data. The first examined the subtest deviations from the scaled score mean, or "test scatter," which is commonly used to evaluate cognitive deficits.[21] The second involved analysis of the absolute test scores to enable standardized measurement of intellectual integrity.

In comparing the WAIS subtest scatter (Figure), the two groups were found to show highly similar profiles (Pearson's $r=.79$, $P<.02$ on initial testing, and Pearson's $r=.91$, $P<.001$ on follow-up). Two notable exceptions, however, were the Comprehension and Digit Span subtests. When analyses were performed to control for overalll IQ, by considering a subject's subtest deviation from his scaled score mean, the LSD psychotics were significantly lower than the schizophrenics on the measure of comprehension ($t=2.26$, $df=40$, $P<.05$), which assesses social judgment and reasoning. By contrast, their scores on digit span, which involves memory and attention and is sensitive to the disruptive effects of anxiety, were significantly higher than the scores of schizophrenics ($t=2.05$, $df=40$, $P<.05$).



Comparison of Wechsler Adult Intelligence Scale (WAIS) subtest pattern by LSD psychotics (solid line) and schizophrenics (broken line) during acute phase. Inf indicates information; Com, comprehension; Ari, arithmetic; Sim, similarities; DSp, digit span; Voc, vocabulary; DSy, digit symbol; PC, picture completion; BD, bock design; PA, picture arrangement.

The global WAIS scores are reported in Table 4. Both groups demonstrated significantly higher verbal than performance IQs ($t=6.35$ and 5.61, respectively, $P<.001$), in keeping with the pattern characteristic in schizophrenia,[21] and the nearly identical degree of disparity between the two scales (13 to 14 points) did not distinguish the patients of the compared groups.

Visual-motor Deficits.—Comparisons on the Bender and Benton tests (Table 4) indicated no differences in visual-motor performance. "Defective" protocols were obtained in a high proportion of both groups. On the Bender, all LSD patients and schizophrenics achieved a score of 45 or greater, which falls into the "organic" classification.[37] Using Benton's criterion of four or more errors on his test,[25] 81.0% of each group could be diagnosed as brain damaged.

Rorschach Scales of Thought Disorder.—As indicated in Table 4, the two groups showed no difference on most Rorschach scales. What distinguished between them, however, was the poorer quality of reasoning (TQ) and greater immaturity of percepts (DL) scored by LSD psychotics. The difference in DL ($F=6.22$, $P<.05$) emerged significant only after adjusting for the somewhat higher Full-Scale WAIS IQs of the LSD group via analysis of covariance. The partialing out of intelligence was necessary to compare developmental levels, as these two factors are reported to be intercorrelated.[38,39]

Patient Characteristics in Test Reports

A comparison of traits identified in the written test evaluations (Table 2) suggested that the LSD patients may be viewed during their first psychotic episode as more passive and chronic than comparable schizophrenics. The latter, alternatively, seemed to show greater signs of confusion, disorientation, dependency needs, and awareness of their impaired functioning.

Follow-up Findings

Course of Illness.—The percentage and distribution of psychiatric rehospitalization over time were remarkably parallel for the two groups (Table 5). Altogether, 11 (52.4%) of the LSD psychotics and ten (47.6%) of the schizophrenics had at least one rehospitalization for psychosis in the three to five years since their first acute admission. Thus, in regard to course of illness, which is considered one of the most relevant criteria for differential diagnosis, there was no significant difference between the two groups.

Cognitive Impairment.—On follow-up, only the schizophrenic comparison group achieved significant gains on the full-scale WAIS (correlated $t=2.37$, $df=20$, $P<.05$), whereas the LSD psychotics exhibited marginal improvement (correlated $t=2.00$, $df=20$, $.10>P>.05$). Most of the gains were on the performance scale, on which only the schizophrenics advanced significantly (correlated $t=2.57$, $df=20$, $P<.02$), whereas the verbal scale revealed no reliable change by either group. Analysis of variance for the Rorschach DL indicated in both groups a significant gain over time since the first hospitalization ($P<.05$) but no significant difference between them in the degree of their improvement.

Table 5.—Incidence of Subsequent Hospitalizations of LSD Psychotics and Acute Schizophrenics Three to Five Years After Initial Illness

	No. of Rehospitalizations					
Clinical Group	0	1	2	3	4	5+
LSD psychotics (n=21)	10	3	5	2	1	0
Schizophrenics (n=21)	11	3	4	2	1	0

COMMENT

The purpose of this work was to provide an objective, multidimensional comparison of LSD-precipitated psychosis with acute schizophrenia. In interpreting the findings, some of the inherent limitations in the design and scope of study need to be considered. Part of the data base derived from retrospective and semistructured methods, which provide a weak (ie, conservative) test of group differences. Thus, the usefulness of case histories is restricted by the questionable accuracy of interviewers and informants, who may be selective or incomplete in assembling data. The interview process used to assess mental status has similar shortcomings, which limit the precision and discriminative power of the ratings, hence increasing the chances of type 2 error. It should also be noted that our study relates only to patients who experienced prolonged LSD psychosis (cf Bowers and Freedman[1]), as distinct from some of the initial panic reactions or immediate toxic effects of LSD that have been described elsewhere.[5,7] Nor have we compared LSD psychotics with nonpsychotic users or those who experience a brief psychotic break, and therefore the differences among these groups cannot be addressed herein. In contrast to other recent investigations (eg, Tsuang et al[40]), the LSD and schizophrenic comparison groups in our study comprised first-admission cases, in whom there was no contamination associated with chronic deterioration or institutional career. At the time of evaluation they had undergone approximately four weeks of hospital treatment with sustained psychotic manifestations.

From the aggregate of results, the patients with prolonged psychotic reaction to LSD emerged as essentially similar to first-break schizophrenics despite some specific differences in parental illness, acute symptoms, cognitive test data, and follow-up assessments.

The family history data found the LSD-induced psychotics indistinguishable from schizophrenics in terms of parental psychosis. This outcome offers a statistical substantiation of earlier descriptive reports that have suggested a "positive family loading" based on smaller samples of drug-related psychotics.[11,12,14,40] Because our data do not specify the nature of psychosis in the families of LSD patients, these can neither confirm nor refute Tsuang et al's findings[40] or Bowers' comparable speculation about the "organismic vulnerability [of LSD casualties] to psychoses with affective features."[12] It should be noted, however, that Tsuang's observation of affective disorder among the parents of long-term psychotics with drug abuse is founded on circumstantial criteria (ie, affective symptoms that abated without leaving significant personality defect). Nevertheless, there

are some indirect clues implicit in our results that would suggest the prevalence of a schizoaffectivelike picture among the LSD psychotics. The somewhat higher frequency of depressive traits and lower frequency of delusions and manifest thought disorder argue in this direction. In addition, the significantly higher proportion of parental alcoholism among LSD psychotics (30.8%) compared with schizophrenics (13.1%) and the population at large (4.5%) could be interpreted as suggestive of an affective component, because following the reasoning of Stone, vulnerability to alcoholism is associated with a manic-depressive genetic loading.[8]

These exceptionally high rates of alcoholism in the parents of LSD patients, comparable with those obtained for parents of alcoholics, further imply a special susceptibility to substance abuse not typical for schizophrenics. In these respects, one may characterize the person who eventually becomes an LSD casualty as one who was initially at high risk for both drug abuse and schizophrenic decompensation in response to the hallucinogen. Whether because of genetic or environmental factors, it would appear that this group premorbidly is more apt to use drugs, perhaps, as a means of coping with life stresses, and also to succumb to schizophrenia under the impact of the LSD experience.

Comparison of premorbid histories with the Phillips scale, however, revealed no group differences in overall level of former adjustment. In this regard, our findings departed from those of Bowers[12] and Breakey et al,[14] whose drug-using patients had better premorbid personalities than controls. Yet curiously, the actual Phillips scores obtained for the drug-related psychotics in Breakey's study (mean, 14.70) were in fact slightly worse than for ours (mean, 13.52). This suggests that the disparity in outcomes traces to differences in the comparison groups studied, ours having been first-break schizophrenics with better premorbid adjustment.

The formal cognitive testing enabled further probe of distinctive features of the LSD psychotics. In analysis of the perceptual-motor impairments, the tests revealed no difference from schizophrenics in "soft signs" of organic brain dysfunction (cf McGlothlin et al[41] and Acord and Barker[42]). Accordingly, there was no obvious toxic influence that could be construed from the test performance. Likewise, on the WAIS the LSD patients were found to be at least as intelligent as the schizophrenic group. However, on this procedure and on the Rorschach test they presented a specific pattern of results that would suggest lesser anxiety, poorer social judgment, greater immaturity of percepts, and more impaired reasoning. On the WAIS profile, for example, they achieved higher scores than schizophrenics on the Digit Span subtest and lower scores on the Comprehension subtest. The first of these measures requires sustained concentration and is vulnerable to interference from acute anxiety. The lesser anxiety among LSD psychotics thus suggested may conceivably reflect an aspect of the predrug personality in common with persons having sociopathic traits. The lower performance on the Comprehension subtest, which is heavily weighted with items relating to social mores and their acceptance, would support this interpretation. Such conclusion would also be congruent with the findings of Hensala et al[11] that among hospitalized LSD psychotics disproportionately many have "antisocial premorbid traits," and of Smart and Jones,[16] who have found test signs indicative of "conduct disorder." In this context, considering the family loading of LSD psychotics for alcoholism, it is of note that alcoholics have also been reported to be distinguished premorbidly by sociopathic tendencies during childhood.[43]

The overall similarity of the test profiles of LSD psychotics and first-break schizophrenics during both the acute phase and the three- to five-year follow-up argues further against viewing these conditions as essentially distinct. If prolonged LSD psychosis were primarily or exclusively related to the drug's toxicity, then the severity of the episode, its course, and test assessments would expectedly reflect less illness than in schizophrenic reactions. Such differences are commonly observed, for example, in experimental trials of LSD by normal subjects still under the immediate influence of the drug.[3] Yet in the present study of prolonged LSD psychotics, the degree of test deficit on admission and follow-up, as well as the rates of rehospitalization, were generally comparable with those for acute schizophrenics. In fact, in the few areas that distinguished these two patient groups, the LSD psychotics appeared to be more impaired. Thus their initial test reports more often alluded to "passivity" and "evidence of chronicity" while less commonly to "sense of impairment" and concern about their own illness. These characteristics suggest a certain ego-syntonicity of symptoms, a presumptive sign of early chronicity. In observing similar trends, Tsuang et al[40] proposed that the greater impairment of drug-induced psychotics may be due to the direct compounding effect of the drug experience. The present results, however, point instead to factors inherent in this particular population associated with their predrug personality and family loading.

In summary, the pattern of results argues against regarding LSD psychosis as a nosologic entity distinct from acute schizophrenia or attributable fundamentally and specifically to toxic drug effects. The emergent clinical features may be understood as an interaction of the acute psychotic decompensation precipitated by the LSD, or whatever crisis situation had motivated its use, with the chronic pathologic premorbid traits of these patients. Preexisting sociopathic characteristics, together with a genealogic predisposition for substance abuse, may have contributed to the involvement with LSD, perhaps as a route of escape from other pressures or, as Blumenfield and Glickman[10] have suggested, as an attempt at self-medication. Considering the high rates of parental psychosis in these patients, it is quite possible that the pharmacologic stressor induced a schizophreniform reaction that in most respects is indistinguishable from non–drug-precipitated schizophrenic conditions.

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