Visual Phenomenology of the LSD Flashback

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• **One hundred twenty-three persons with a history of LSD use were studied for the presence of the LSD flashback phenomenon and compared with 40 control subjects. A syndrome emerged that included ten distinct visual disturbances. It had lasted for five years in half of the population, was treatable with benzodiazepines, exacerbated by phenothiazines, and precipitated by 19 different stimuli, most commonly emergence into a dark environment. Sensitivity to LSD as determined by flashbacks appears to divide the study sample into three discrete subgroups. There may be a genetic basis to LSD sensitivity.**

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The task of defining the nature of long-term effects of drug abuse is fraught with difficulty.[1] Confusion often reigns because of a variability in samples, drug types and dosages, preexisting psychopathology, physical illness, and a diversity of diagnostic and outcome measures. The study of human effects from the hallucinogen LSD is compounded further by a wide variability of responses to the drug at the same doses.[2]

With the aforementioned as preamble, it is noteworthy that a number of long-term sequelae have been attributed to the use of LSD. They include a thought disorder,[3] subtle changes in the EEG,[4] a decrease in higher cortical functions,[5] abnormal Minnesota Multiphasic Personality Inventory results,[6] an abnormality in color perception,[7] a decrease of the serotonin catabolite 5-hydroxyindoleacetic acid (5-HIAA) in the CSF of psychotic subjects with prior LSD use,[8] and psychosis.[9,10] A ten-year follow-up study of medical LSD use in psychiatric outpatients and volunteers, however, failed to find evidence of lasting psychologic effects.[11] The reported deviant response to the Reitan trail-making test among collegiate LSD users[12] was not found among healthy adults.[13]

In 1955 Elkes et al[14] were among the first to suggest that LSD might have long-term effects in man. In 1958 Eisner and Cohen[15] reported the spontaneous appearance of LSD phenomena at varying intervals following exposure, which were described by their patients "as relaxing and beneficial." Rosenthal[16] presented evidence that visual hallucinations might last as long as five months from the time of last exposure. Cohen and Ditman[17] reported a series of nine LSD users with prolonged effects from the drug lasting as long as two years.

Although to date there has been no systematic inventory of the types of visual disturbances experienced chronically in this population, Horowitz[18] made one of the earliest efforts in this direction, reporting on 31 subjects with long-term LSD use who described three distinct visual types of flashbacks: perceptual distortions, heightened imagery, and recurrent unbidden images. In addition to perceptual changes, Shick and Smith[19] described somatic and emotional flashbacks. Of special note is that although six reports[11,16,18-21] proposed that such disturbances only appeared in subjects having multiple exposures, three studies[11,18,22] failed to find statistically significant differences in such disturbances between heavy and light LSD users, and several observers found flashbacks after a single LSD exposure (D. X. Freedman, MD, written communication, Oct 14, 1981).[19] One report[11] suggested that visual disturbances and LSD use "seem to be nothing more than the association of two events bearing certain similarities." While the dose-response characteristics have been unclear in the literature, reports on the incidence and severity of such visual disturbances also vary widely. Accordingly, the prevalence of flashbacks in populations of LSD users has varied from 15%[11] to 77%.[23]

Precipitants of such recurrences have not been studied systematically. A theory that such disturbances are linked to stress[16,18,19] was not supported by a survey of LSD users before and after military combat.[22] Though evidence shows that LSD interacts acutely with diverse regions of the CNS,[24] and while the drug clearly appears in high concentration along visual pathways,[25] no evidence has been presented that clarifies whether the drug operates at any CNS site on a long-term basis. Of special note is the association between LSD-type flashbacks and the use of marijuana. Six separate reports[19,26-30] linked flashbacks to marijuana use, but in each report the subjects described an antecedent use of LSD that also explained the flashback. Further data from the survey of 720 servicemen[30] in western Europe failed to find a single case of flashbacks in any subject for whom hashish was the sole drug of consumption. In the same sample, however, 15 subjects were found for whom LSD flashbacks were precipitated by marijuana use. Another military sample of 2,001[29] discovered that marijuana use had the highest, and only, significant association with the precipitation of LSD flashbacks among five classes of abused substances.

Finally, treatment data are contradictory. Moskowitz[31]

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treated eight subjects for flashbacks successfully with haloperidol, Anderson and O'Malley[32] found trifluoperazine hydrochloride useful in one case, but Schwarz[33] reported that chlorpromazine given to two subjects during acute LSD experiences exacerbated visual symptoms. A report by Thurlow and Girvin[34] offered evidence that an anticonvulsant, phenytoin, was helpful in a single case. The consensus of a number of clinicians, however, has been that neuroleptics are not the treatment of choice.[19,35]

But what are the types of visual disturbances chronically experienced by these individuals? How long after the last use of LSD do such disturbances appear? What precipitates them? Do the disturbances correlate with other drugs of abuse? If so, which ones? And what about treatment? Which is effective? Can the phenomenon of the flashback teach us anything about which regions of the brain are involved in these hallucinatory phenomena? And most importantly, what is the basis of the great variety of responses to LSD in the medical literature? Some of these questions are approached in the following study, which focuses on the phenomenology of the LSD flashback, its precipitants, treatments, and clinical course.

SUBJECTS AND METHODS

Following a decade-long epidemic of drug abuse in the 1960s in the United States, the Department of Psychiatry at the Massachusetts General Hospital, Boston, began treating a variety of persons who were casualties of that experience. The department operates a walk-in psychiatric emergency service that treats approximately 200 patients per week. From 1971 to 1974, 123 subjects with one or more self-reported exposures to LSD were found who gave informed consent for the study.

Fifty-three subjects were chosen consecutively in the first phase. All subjects were referred to the study in response to a single notice in the Acute Psychiatric Service requesting "any person having used LSD." No request was made for subjects with clinical problems allegedly linked to LSD. All referrals were made by residents in the Department of Psychiatry in two settings, the acute service and the inpatient unit. The subjects were predominantly white, male, unemployed, with less than a year of college, and with drug abuse as the most common diagnosis. The ratio of outpatients to inpatients was 6:1. Inclusion criteria were (1) a history of at least one exposure to LSD and (2) a description from the subject of a characteristic response, ie, a toxic psychosis with predominantly perceptual and/or affective changes lasting six to 12 hours following the ingestion of an odorless, tasteless compound in an epidemiologically recognizable form (eg, sugar cube, blotter). Included were subjects who had ingested "mescaline," but excluded were all subjects who claimed only to have used other strong hallucinogens, or whose conditions were diagnosed as organic brain syndrome, seizure disorder, migraine, cerebral trauma, or a history of CNS tumor or infection. In addition, no subject was included who at the time of the interview was in a toxic state from any drug or drug withdrawal. Subject selection in the study predated popular abuse of phencyclidine. A chemical analysis of street drugs at the time our subjects were using LSD found that the likelihood of street samples actually being LSD was 80.3%.[36] McGlothlin and Arnold[11] reported subjective estimated doses of nonmedical LSD for the same period in the range of 50 to 1,000 μg, with a median dose of 125 μg per exposure. A median dose for street LSD samples at that time ws confirmed at an estimated 100 μg by the Massachusetts Department of Public Health (R. Timperi, MPH, oral communication, Sept 1, 1982). The author had no reason to believe the dosages in the study sample were substantially different.

First Phase

Subjects in the first phase were subjected to unstructured interviews regarding all conditions they considered sequelae of the use of LSD. All interviews were conducted by me, took place in the Acute Psychiatric Service, and lasted one hour. A cornucopia of perceptual data was uncovered that was alleged to be related to past drug experiences. In addition, complaints included such diverse items as insomnia, psychosis, stammering, vertigo, dyslexia, violence, photophobia, and precognition, all of which were said to occur weeks to years following the last exposure to LSD. Of these many symptoms, 16 visual disturbances most compatible with those reports in the literature of the generic class "flashback" were chosen for closer study. The clinical description of these subjects follows.

Acquired Color Confusion.—Excluded from this category[7] were reports from subjects with a history of congenital color blindness. Included were reports from subjects from whom the color of objects changed or presented a newly discovered problem of color confusion. One subject in this phase of the study had trouble in his job as a shoe salesman because he confused dark brown with navy blue, and tan with beige.

Difficulty Reading.—Excluded were reports of dyslexia predating drug use. A number of subjects reported the insidious onset of trouble reading that appeared relatable to a variety of complaints, including a loss of concentration, a lack of motivation, a confusion by the content of texts, and the intrusion of visual disturbances such as positive and negative afterimages of the type against the background of the page. Several complained that this last phenomenon would create a bichromatic alphabet soup of images that made study difficult.

Flashes of Color.—Unexpectedly and without apparent stimulus, a subject would experience the flash of a bright color across the visual field of both eyes.[37] It often was described as a sheet of light or a rapidly appearing and disappearing mist.

Geometric Pseudohallucinations.—Subjects commonly reported seeing geometric figures come and go before their eyes both when open and closed.[16,31,38,39] No subject believed these figures were real events, and so the term *pseudohallucination* was more appropriate in describing these phenomena.[40] Examples included "sparkles," which were described as visual fireworks, coming in bursts and consisting of hundreds at a time. Also described were lattices; colored, transparent doughnut-shaped images; large, transparent blobs that floated indefinitely in one's visual field; and complex geometric patterns arising from no known primary stimuli.

Geometric Phosphenes.—Phosphenes, or eigengrau, are nonspecific luminous perceptions that occur when the eyes are closed, and may originate from entopic stimuli (arising from within the eye itself) in normal persons. They also may be induced by gentle pressure on a closed eyelid.[41] The usual description in normal subjects of such phenomena may be diffuse areas of brightness, the patterns of one's eyelashes, or the intimation of a more formed image, such as concentric circles or swirls. Such descriptions of visual phenomena were not counted in this study. Instead, I included subjects reporting formed, stable, unambiguous geometric images with eyes closed, with or without digital pressure on the globes. Commonly reported were the geometric pseudohallucinations described previously. Of special note was the report of one subject who saw "sprinkles" of colored light in one open eye whenever he rubbed his closed, opposite eye. Another subject reported hundreds of 1-cm dots with eyes closed whenever he coughed severely.

Halos Around Objects.—Halos[19] tended to occur under photopic conditions indoors. One subject reported seeing a halo about the researcher's arm and head. Another noted a similar mist surrounding an office telephone. Many times it was not possible to distinguish halos from mists.

Illusions of Movement.—Subjects often reported imagining that a stable object appeared to wave, roll, or jump.[18,19,22] These phenomena appeared to occur so much more in the peripheral visual fields that they came to be known in the study as PIPs, an acronym for "perceptions in the periphery." One subject reported that an office flower pot appeared to slide across the windowsill when viewed from the corner of her eye. A second subject saw the floor appear to fall away from him and suffered concomitant vertiginous attacks and falling.

Imagistic Phosphenes.—These are phosphenes of unbidden, formed images (not geometric patterns) generated on closing an eye or pressing it with a finger. Two subjects within the first week of an LSD exposure were able to see such images when the researcher exerted gentle digital pressure on the eyes. One saw

Table 1.—Characteristics of the Study Sample

Variables	LSD Users	Control Subjects
Mean No. of lifetime LSD exposures	164±28	0
Median No. of lifetime LSD exposures	75	0
Mean time from last LSD use, yr	1.9±0.3	0
% Male	78.6	75.0
% White	97.1	94.7
Mean age, yr	22.4±4.2	28.0±12.3
% With history of psychosis	22.9	20.0
% Single	84.1	76.5
Highest educational level, yr	12.8±2.8	14.5±5.1
No. in household	2.2±2.4	2.3±2.0

"the face of God," and the second, "a Mickey Mouse cartoon."

Intensified Colors.—Subjects reported looking at the normally saturated color of an object and then watching it take on an abrupt, vivid brightness lasting for a few seconds.[18]

Macropsia.—Macropsia[18,40] is the perception of an object larger than it really is. A characteristic description of this phenomenon came from a subject who noticed that his hand was enormous and then of normal size a few seconds later.

Micropsia.—Micropsia[18,40] is the perception of an object smaller than reality. One subject said, "My feet looked so tiny, like they were a million miles away."

Negative Afterimages.—This occurs when an image the complementary color of the primary stimulus is seen after the primary stimulus is gone.[42] For example, a subject reported that she could look at the blue type on a page and see a yellow image of it floating between the lines.

Pareidolias.—This is literally an image within an image.[40] These were described when a subject gazed into a finely reticulated design in linoleum, veneer, or a cloud formation. Besides the abstract pattern of the linoleum, subjects often would be able to see a series of concrete images as well, such as "a fish," "a face," and "a little boy."

Positive Afterimages.—These are images the same color as the primary stimulus.[42] Subjects reported they could see the "blue shadow" of a blue pen that floated as an aerial image on a wall or door.

Trailing Phenomena.—"Trails" have been described previously in patients using LSD.[32] These are formed, positive afterimages that remain immediately behind an object as it moves across the subject's visual field. Testing for trails was done as follows. With arms folded across the chest (to avoid any nonverbal gesture that would bias the answer) the examiner asked the subject if he or she ever "saw any trails." Often, when the subject was particularly experienced with hallucinogens, he or she would wave a hand across the visual field and say, "Oh, you mean these?" The subject could then describe a trail of images of the moving hand, much like the frames of a piece of motion picture film frozen in space long enough for the subject to see them. Trailing was considered present if the subject could describe this phenomenon as part of a past or present hallucinogen-free experience.

Second Phase

For the second phase of the study subjects again were referred by residents in response to a notice in the Acute Psychiatric Service. Criteria for subject selection in the second phase were the same as in the first phase. Seventy persons with a history of using LSD at least once were found. The typical subject was a 23-year-old, single, white male psychiatric outpatient with one year of college who had exposures to LSD for a mean of 96 separate occasions, but with no use in the two years preceding the interview. He was not likely to have had a history of psychiatric hospitalization, but his condition was likely to have been diagnosed as drug dependent. Seventeen percent of the LSD users in the second phase comprised a cohort of staff volunteers from three Boston-area hospitals who had expressed an interest in the project and were interested in providing data on the consequences of self-experimentation with hallucinogens.

Table 2.—Lifetime Drug Abuse Other Than LSD

Drug Type	Inclusion Criterion	% of LSD Users (N=70)	% of Controls (N=40)	P*
Narcotics	History of addiction and withdrawal	21.5	2.6	.0195
Marijuana	More than once a day	27.9	8.3	.0416
Amphetamines	More than 1 wk continuously	25.4	13.2	NS
Alcohol	One or more CAGE criteria for problem drinking[61]†	41.4	42.5	NS
Hypnosedatives	History of addiction and withdrawal	6.3	0	NS
Cocaine	History of addiction and withdrawal	3.1	0	NS

*A 2×2 corrected χ^2 test was used to calculate P values.

†The CAGE criteria score one point for each of the following: (1) a history of cutting down one's drinking; (2) annoyance by criticism over one's drinking; (3) guilt over drinking; and (4) using alcohol as a morning "eye opener."

In addition, a control group of 40 subjects was matched to the LSD sample for the variables of age, race, sex, marital status, educational level, size of household, and history of psychotic disorders. They differed from the LSD group in that they denied any history of using any strong hallucinogen. Characteristics of the study sample are tabulated in Table 1.

Drug histories were taken on each subject's life experience regarding hallucinogens, marijuana, narcotics, hypnosedatives, amphetamines, cocaine, and alcohol. A summary of these data is shown in Table 2.

An 83-item questionnaire was constructed that incorporated the 16 visual disturbances most commonly reported in the first phase. The information fell into six categories: (1) psychiatric and social history; (2) psychiatric diagnoses and treatments; (3) visual disturbances, their causes, and treatments; (4) other flashback symptoms and treatments; (5) other drug history scored as continuous variables; and (6) a history of the subject's lifetime use of LSD from its inception to last exposure. Also included was a "trip-by-trip" analysis of the subject's use of LSD in an effort to calculate a lifetime dose. Since "mescaline" had been found previously to be LSD when chemically assayed,[43] such trips were included in the final tally for each subject. Life doses from each subject then were segregated into cells arranged at the following intervals: one to ten trips, 11 to 20, 21 to 30, 31 to 40, 41 to 50, 51 to 75, 76 to 100, 101 to 300, 301 to 500, and greater than 500 LSD exposures over a lifetime. This life dose served as an abscissa against which the dependent variables of visual disturbances and flashbacks could be graphed as ordinates. In addition, 22 subjects were referred for a battery of psychophysical tests that included kinetic perimetry, color vision, flicker perimetry, dark adaptation, perception under glare, and a test of simultaneous color contrast, results of which are reported separately.[7] Following the questionnaire, subjects also were interviewed in an unstructured fashion for approximately one hour, usually in the setting of the Acute Psychiatric Service.

Completed data were recorded for 89% of the sample. Incompletions were due largely to the clinical needs of the patients who required hospitalization, crisis intervention, or whose answers were excluded by virtue of prepossessing delusions or hallucinations. This biased the sample toward the healthier subjects, but also toward the more reliable ones.

RESULTS

Of the 70 subjects with a history of LSD use, 53.5% of the sample reported subjective symptoms, which they labeled "flashbacks," a week or more following last exposure to the drug. The mean number of visual disturbances among LSD users was 4.8 ± 3.0 per subject, compared with 1.8 ± 3.0 among the control subjects ($P<.001$).

Table 3.—Ranked Frequency of Visual Disturbances Associated With Prior LSD Use

Type of Disturbance	% of LSD Users (N=70)	% of Controls (N=40)	P*
Geometric pseudohallucinations	58.6	2.5	<.0001
Perceptions in peripheral field	57.1	10.0	<.0001
Flashes of color	44.3	5.0	<.0001
Intensified colors	40.0	2.5	<.0001
Trailing phenomena	44.3	5.4	.0001
Imagistic pseudohallucinations	42.9	7.5	.0002
Positive afterimages	28.6	2.5	.002
Halos around objects	27.1	5.0	.0096
Macropsia	21.4	5.0	.0435
Micropsia	17.1	2.5	.0435
Geometric phosphenes	20.0	20.0	NS
Imagistic phosphenes	20.0	7.5	NS
Pareidolia	18.6	12.5	NS
Color confusions	17.1	12.5	NS
Negative afterimages	15.7	7.5	NS
Difficulty reading	12.9	7.9	NS

*A 2×2 corrected χ^2 test was used to calculate P values.

Table 4.—Pearson's Correlation Coefficients Between Drugs and Visual Disturbances

Drug Abused	Correlation	P*
LSD	.321	.001
Marijuana	.291	.005
Alcohol	.151	NS
Amphetamines	.058	NS
Cocaine	.012	NS
Hypnosedatives	.004	NS
Narcotics	−.027	NS

*A two-tailed test was used to calculate P values.

Table 3 ranks the kinds of visual disturbances encountered by the sample. A core of visual disturbances, most commonly including geometric and imagistic pseudohallucinations, illusions of movement, trails, flashes of color, and the prolonged intensification of color, emerged from the data. Pearson's correlation between the presence of these visual disturbances and a clinical description of flashbacks by the subjects was .586 ($P<.001$).

Association Between Visual Disturbances and Past LSD Use

Figure 1 illustrates the relationship between the total number of reported LSD exposures at ten dose levels and the percentage of flashbacks of subjects in each level with a clinical appearance of flashbacks. The hypothesis that there is a linear relationship between LSD life dose and flashbacks was rejected. What appears, instead, is a relationship between dose and response that has a peak at 15 exposures, a second peak at approximately 40 exposures, and a plateau thereafter. Table 4 illustrates Pearson's correlation coefficients for LSD and all drugs listed in Table 2 against the total number of reported visual disturbances using data from LSD users and control subjects. The greatest correlation is for LSD, and the least for narcotics. Also, there was a weak but significant trend between visual disturbances and marijuana use. It is noteworthy that while LSD has the highest correlation with visual disturbances in this sample, coefficients for other drugs of abuse fall in the general order that one would expect regarding their respective abilities to stimulate visual perceptions.

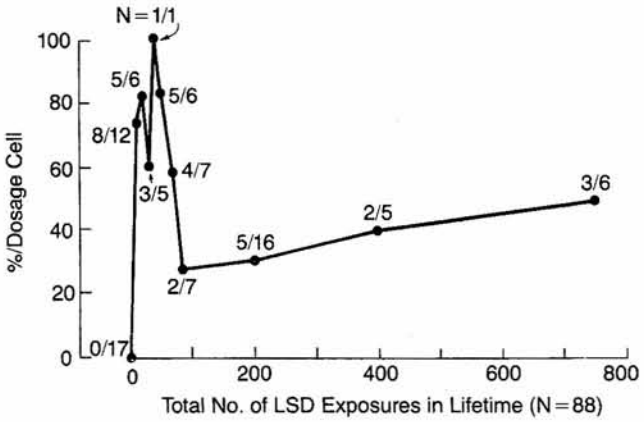

Fig 1.—Life histories of total LSD exposures were recorded in sample, and ten groups were formed according to numbers determined. "Dosage cells" were plotted against percentage of subjects in each group with clinical diagnosis of LSD flashbacks. Using analysis of variance, $F=3.53$; $P<.01$.

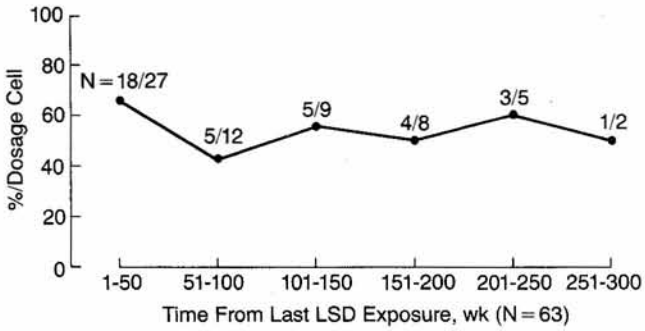

Fig 2.—Percentage of LSD users with flashbacks was plotted as function of six time intervals from last use of drug.

Stability of the Visual Disorder in Time

Figure 2 illustrates the relative stability of visual disturbances in the user population over a five-year span. The hypothesis that all such disturbances disappear in time was rejected, since approximately half the users in each time interval from last drug exposure continued to report flashbacks at the time of the interview.

Precipitants of Visual Disturbances

Table 5 itemizes 19 separately reported precipitants of visual disturbances following the use of LSD. The most common precipitant is the emergence into a dark environment in 16% of the users. Characteristically, a subject described entering a dwelling after being outdoors for a number of minutes or longer. Once indoors the subject described a variety of disturbances, the most common being geometric pseudohallucinations. Another common precipitant was intention in 14%. Subjects intentionally induced visual aberrations by staring at a blank wall or blackboard.

Fourteen percent of the users also reported that marijuana could precipitate LSD-type flashbacks. A further examination of 15 control subjects with a history of heavy marijuana use ("more than once a day") revealed that none of the subjects ever reported experiencing any flashback phenomena, while seven of 12 LSD users with the same marijuana history did report flashbacks ($P=.003$). This finding strengthens a reportedly unique form of drug-drug interaction between LSD and marijuana, though the evidence to date remains solely based on clinical histories.

Treatment of Visual Disturbances

Twenty-one patients with visual disturbances were treated for flashbacks and/or psychotic disorders. Nine subjects received benzodiazepines and 12, phenothiazines. Of the nine receiving the

Table 5.—Ranked Frequency of Reported Precipitants of Visual Disturbances

Type of Agent	No. of Reports (N=70)	%
Emergence into a dark environment	11	16
Intention	10	14
Marijuana	10	14
Phenothiazines	9	13
Anxiety	8	11
Fatigue	8	11
Amphetamines	6	9
Alcohol	5	7
Phosphenes from pressure on closed eyes	5	7
Exercise	4	6
Alcohol withdrawal	2	3
Antiparkinsonian drugs	2	3
Cold tablets	2	3
Narcotics withdrawal	2	3
Antidepressants	1	1
Barbiturate withdrawal	1	1
Diazepam	1	1
Noise	1	1
Sexual intercourse	1	1

former, eight reported that the medication reduced the intensity and frequency of visual disturbances, whereas 11 of the 12 subjects receiving phenothiazines reported a transient but definite exacerbation of visual disturbances as defined in Table 3 ($\chi^2=13.63$; $P<.001$). Other remedies improving visual disturbances were narcotics in two cases, sunglasses in two, barbiturates in one, and alcohol in one. Treatment data will be reported separately.

COMMENT

It appears that LSD can be associated with a chronic, irreversible, or slowly reversible collection of visual disturbances in a sample of heavy LSD users that largely included psychiatric outpatients but also included a number of otherwise normal volunteers. Such disturbances most commonly were geometric pseudohallucinations, illusions of movement in the peripheral visual field, trailing phenomena, flashes of color, imagistic pseudohallucinations, and intensified colors for brief periods of time. Other visual symptoms may be present, but these occurred in 28% or less of the study sample.

Of note is that while 12.9% of the sample sought clinical help for flashbacks, 32.9% reported considerable numbers of visual symptoms (more than an SD beyond the control mean), usually of a mild nature, suggesting that the LSD flashback in this sample may represent a more pronounced species of a broader range of drug-related perceptual disorder. With this in mind, one may construct a working definition of an LSD flashback as the recapitulation of an LSD-like subjective experience, often but not always in the form of altered visual perceptions occurring weeks to years following an exposure to the drug. In the present sample such disturbances were invariably pseudohallucinations rather than perceived and believed hallucinated imagery.

While such visual disturbances can be striking, no generalization can be made about the population of LSD users at large. The sample was drawn in large measure from an acute psychiatric outpatient population and, though steps were taken to minimize a bias toward the selection of LSD casualties, selection could not utterly escape that bias. In addition, a retrospective study of flashbacks faces formidable problems in the reliability of self-reports; the kind and dose of the drug abused; and the confounding of variables by such factors as intelligence, personality, and preexisting psychopathology. It is, however, the unique, consensual reportage that makes the foregoing observations appear to be valid.

The observation that emergence into a dark environment is one of the most common precipitants of these disturbances suggests that the neurophysiologic basis of flashbacks may be related to a failure of an inhibitory system of the visual pathway to function properly. Such a locking of visual circuitry into an "on" position following perception of a visual stimulus would explain such diverse complaints as trailing, color intensification, positive afterimages, phosphenes, and color confusions, each of which may represent a failure of the respective visual function to turn off the brain's response to the stimulus once the stimulus is gone. This would also explain the disparate reportage between positive afterimages (28.6%) and negative ones (15.7%). The latter are induced commonly by a depletion of visual pigment in retinal color receptors, whereas one mechanism for inducing the former may be mediated within the lateral geniculate nucleus (LGN) of the thalamus.[44] If the LGN were a target organ for LSD toxicity, one would expect to find LSD-sensitive neurons there, which, in fact, has been reported.[45,46]

Strengthening the suggestion that visual disturbances are mediated centrally, and not only in the retina, are the subjective reports of several subjects who were able to elicit geometric pseudohallucinations in one eye by putting digital pressure on the other eye. Others at times described a pseudohallucination of one or more circular images, at times a doughnut with an outer ring of one color and an inner ring of a second color. In the macaque monkey's LGN there have been found on-off color neurons[47] with receptive fields similar to those described by subjects with LSD flashbacks, with sizes ranging from 1/32° to 1°, not significantly different from the sizes reported by the present sample of subjects. It is intriguing to hypothesize that some LSD flashbacks may occur from within the LGN and represent episodes of visual seizures. In view of this study's finding of the effectiveness of diazepam, the idea does appear inconsistent with the evidence. A review of Moskowitz's use of haloperidol, furthermore, showed that seven of his eight patients suffered an increase in flashbacks the first week of treatment ($P<.001$), a phenomenon observed by my sample as well. Dovetailing with these findings are reports that low-potency phenothiazines may reduce the seizure threshold.[48] Such a mechanism may also explain the hallucinations of more complex, representational imagery by disinhibition of loci within the cerebral cortex.

It has been suggested previously that LSD has the ability to disrupt defensive and perceptual constancies by which we order our lives.[35] Such habits of perception have been classified into perceptual "types" reflecting character traits.[49,50] While this concept remains controversial, LSD flashbacks may be modulated by perceptual style and psychobiologic maturity. Flashback phenomena, then, appear to operate at multiple levels of organization of the CNS and may be conceptualized productively by models of sensitization and habituation,[24,51-54] neurobehavioral and cellular processes,[55] state-dependent learning,[56] cortical arousal,[57] information processing,[58] and psychodynamics.[35]

The observations of a variegate sensitivity to LSD are confirmed by these data. Figure 1 suggests that the study group is composed of three distinct populations of users: a

group that reports flashbacks at 15 exposures and appears to be extremely sensitive to the drug; a second group with a peak at 40 to 50 lifetime exposures, which is moderately sensitive; and a third group that appears relatively resistant to LSD even at high exposures. The most intriguing hypothesis this observation generates is that in the study sample there exists a genetic basis for variable sensitivities to LSD. Such a sensitivity to the aftereffects of LSD has been proposed previously,[59] and a familial history of major mental disorders reportedly is linked to the frequency of chronic psychotic disturbances after LSD use.[60]

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References

1. Halikas JA: Marijuana use and psychiatric illness, in Miller LL (ed): *Marijuana, Effects on Human Behavior.* New York, Academic Press Inc, 1974.

2. Terrill J, Savage C, Jackson DD: LSD, transcendence and the new beginning. *J Nerv Ment Dis* 1962;135:425-439.

3. Tucker GJ, Quinlan D, Harrow M: Chronic hallucinogenic drug use and thought disturbance. *Arch Gen Psychiatry* 1972;27:443-447.

4. Blacker KH, Jones RT, Stone GC, et al: Chronic users of LSD: The acidheads. *Am J Psychiatry* 1968;125:341-351.

5. Acord LD, Barker DD: Hallucinogenic drugs and cerebral deficit. *J Nerv Ment Dis* 1973;156:281-283.

6. Keller J, Redfering DL: Comparison between the personalities of LSD users and non-users as measured by the Minnesota Multiphasic Personality Inventory. *J Nerv Ment Dis* 1973;156:271-277.

7. Abraham HD: A chronic impairment of colour vision in users of LSD. *Br J Psychiatry* 1982;140:518-520.

8. Bowers MB Jr: Acute psychosis induced by psychotomimetic drug abuse: II. Neurochemical findings. *Arch Gen Psychiatry* 1972;27:440-442.

9. McLellan AT, Woody GE, O'Brien CP: Development of psychiatric illness in drug abusers: Possible role of drug preference. *N Engl J Med* 1979;301:1310-1314.

10. Abraham HD: Psychiatric illness in drug abusers. *N Engl J Med* 1980;302:868-869.

11. McGlothlin WH, Arnold DO: LSD revisited: A ten-year follow-up of medical LSD use. *Arch Gen Psychiatry* 1971;24:35-49.

12. Culver CM, King FW: Neuropsychological assessment of undergraduate marihuana and LSD users. *Arch Gen Psychiatry* 1974;31:707-711.

13. McGlothlin WH, Arnold DO, Freedman DX: Organicity measures following repeated LSD ingestion. *Arch Gen Psychiatry* 1969;21:704-709.

14. Elkes C, Elkes J, Mayer-Gross W: Hallucinogenic drugs. *Lancet* 1955;268:719.

15. Eisner BG, Cohen S: Psychotherapy with lysergic acid diethylamide. *J Nerv Ment Dis* 1958;127:528-539.

16. Rosenthal SH: Persistent hallucinosis following repeated administration of hallucinogenic drugs. *Am J Psychiatry* 1964;121:238-244.

17. Cohen S, Ditman KS: Prolonged adverse reactions to lysergic acid diethylamide. *Arch Gen Psychiatry* 1963;8:475-480.

18. Horowitz MJ: Flashbacks: Recurrent intrusive images after the use of LSD. *Am J Psychiatry* 1969;126:565-569.

19. Shick JF, Smith D: Analysis of the LSD flashback. *J Psychedelic Drugs* 1970;3:13-19.

20. Robbins E, Frosch W, Stern M: Further observations on untoward reactions to LSD. *Am J Psychiatry* 1967;124:393-395.

21. Blumenfield M: Flashback phenomena in basic trainees who enter the US Air Force. *Military Med* 1971;136:39-41.

22. Stanton MD, Bardoni A: Drug flashbacks: Reported frequency in a military population. *Am J Psychiatry* 1972;129:751-755.

23. Holsten F: Flashbacks: A personal follow-up. *Arch Psychiatr Nervenkr* 1976;222:293-304.

24. Freedman DX, Van Praag HM, Lader MH, et al: Mode of action of hallucinogenic drugs, in Van Praag HM, (ed): *Handbook of Biological Psychiatry.* New York, Marcel Dekker Inc, 1981, pt 4, pp 859-884.

25. Snyder SH, Reivich M: Regional localization of lysergic acid diethylamide in monkey brain. *Nature* 1966;209:1093-1095.

26. Smith DE: The acute and chronic toxicity of marijuana. *J Psychedelic Drugs* 1968;2:37-47.

27. Favazza A, Domino E: Recurrent LSD experiences (flashbacks) triggered by marijuana. *Univ Mich Med Center J* 1969;35:214-216.

28. Weil AT: Adverse reactions to marijuana. Classification and suggested treatment. *N Engl J Med* 1970;282:997-1000.

29. Stanton MD, Mintz J, Franklin RM: Drug flashbacks: II. Some additional findings. *Int J Addict* 1976;2:53-69.

30. Tennant FS, Groesbeck CJ: Psychiatric effects of hashish. *Arch Gen Psychiatry* 1972;27:133-136.

31. Moskowitz D: Use of haloperidol to reduce LSD flashbacks. *Military Med* 1971;136:754-757.

32. Anderson W, O'Malley J: Trifluoperazine for the trailing phenomenon. *JAMA* 1972;220:1244-1245.

33. Schwarz CJ: Paradoxical responses to chlorpromazine after LSD. *Psychosomatics* 1967;8:210-211.

34. Thurlow HJ, Girvin JP: Use of antiepileptic medication in treating 'flashbacks' from hallucinogenic drugs. *Can Med Assoc J* 1971;105:947-948.

35. Freedman DX: On the use and abuse of LSD. *Arch Gen Psychiatry* 1968;18:330-347.

36. Marshman JA, Gibbons RJ: A note on the composition of illicit drugs. *Ontario Med Rev* 1970;37:429-441.

37. Scott ME: The flashback phenomenon. *Va Med Monthly* 1971;98: 317-320.

38. Siegel RK, Jarvik ME: Drug-induced hallucinations in animals and man, in Siegel RK, West LJ (eds): *Hallucinations.* New York, John Wiley & Sons Inc, 1975, pp 81-162.

39. Klüver H: *Mescal and Mechanisms of Hallucinations.* Chicago, University of Chicago Press, 1966.

40. Hamilton M (ed): *Fish's Clinical Psychopathology.* Baltimore, Williams & Wilkins Co, 1974.

41. Ladd-Franklin C: Visible radiation from excited nerve fiber: The reddish blue arcs and the reddish blue glow of the retina. *Science* 1927; 66:239-241.

42. Murch GM: *Visual and Auditory Perception.* New York, Bobbs-Merrill Co Inc, 1973.

43. Cheek FE, Newell S, Joffee M: Deceptions in the illicit drug market. *Science* 1970;167:1226.

44. DeValois RL, Smith CJ, Kitai ST, et al: Response of single cells in monkey lateral geniculate nuclei to monochromatic light. *Science* 1958; 127:238-239.

45. Evarts EV, Landau W, Freygang E, et al: Some effects of lysergic acid diethylamide and bufotenine on electrical activity in the cat's visual system. *Am J Physiol* 1955;182:594-598.

46. Bishop PO, Field G, Hennessy BL, et al: Action of d-lysergic acid diethylamide on lateral geniculate synapses. *J Neurophysiol* 1958;21:529-549.

47. Daw NW: Neurophysiology of color vision. *Physiol Rev* 1973;53: 571-611.

48. Baldessarini RJ: Drugs used in the treatment of psychoses, in Goodman LS, Gilman A (eds): *The Pharmacological Basis of Therapeutics.* New York, MacMillan Publishing Co Inc, 1980, chap 19.

49. Vernon MD: *The Psychology of Perception.* Hammondsworth, England, Penguin Books Ltd, 1973, p 202.

50. Shapiro D: *Neurotic Styles.* New York, Basic Books Inc, 1965, p 2.

51. Freedman DX, Aghajanian GK, Ornitz EM, et al: Patterns of tolerance to lysergic acid diethylamide and mescaline in rats. *Science* 1958;127:1173-1174.

52. Isbell H, Belleville RE, Fraser HF, et al: Studies on lysergic acid diethylamide (LSD-25): I. Effects in former morphine addicts and development of tolerance during chronic intoxication. *Arch Neurol Psychiatry* 1956;76:468-478.

53. Davis M, Sheard MH: Habituation and sensitization of the rat startle response: Effects of raphé lesions. *Physiol Behav* 1974;12:425-431.

54. Brunelli M, Castellucci V, Kandel ER: Synaptic facilitation and behavioral sensitization in *Aplysia:* Possible role of serotonin and cyclic AMP. *Science* 1976;194:1178-1181.

55. Halaris A, Freedman DX: Vesicular and juxtavesicular serotonin: Effects of lysergic acid diethylamide and reserpine. *J Pharmacol Exp Ther* 1977;203:575-586.

56. Fischer R: The 'flashback': Arousal-statebound recall of experience. *J Psychedelic Drugs* 1971;3:31-39.

57. Winters WD: The continuum of CNS excitatory states and hallucinosis, in Siegel RK, West LJ (eds): *Hallucinations.* New York, John Wiley & Sons Inc, 1975, pp 53-70.

58. Horowitz MJ: Hallucinations: An information processing approach, in Siegel RK, West LJ (eds): *Hallucinations.* New York, John Wiley & Sons Inc, 1975, pp 163-196.

59. Bowers MB Jr: Serotonin (5HT) systems in psychotic states. *Psychopharmacol Community* 1975;1:655-662.

60. Tsuang MT, Simpson JC, Kronfol Z: Subtypes of drug abuse with psychosis: Demographic characteristics, clinical features, and family history. *Arch Gen Psychiatry* 1982;39:141-147.

61. Ewing JA: Identifying the hidden alcoholic. Read before the 29th Congress on Alcohol and Drug Dependence, Sydney, Australia, Feb 3, 1970.