Journal of Abnormal Psychology
1988, Vol. 97, No. 4, 443–447

0021-843X/88/$00.75

Visual Function in Past Users of LSD: Psychophysical Findings

Henry David Abraham
Department of Psychiatry
Harvard Medical School

Ernst Wolf
Psychophysics Laboratory
Eye Research Institute of the Retina Foundation

Twenty-four subjects with a history of use of the hallucinogenic drug, LSD, 2.3 years prior to being studied were found on psychophysical testing to have impairments of visual function when compared with a matched control group. The LSD group had depressed critical flicker frequencies ($p < 0.0001$) and reduced sensitivity to light during dark adaptation ($p < 0.0001$). Peripheral visual fields appeared to be predominantly affected. Drug effects were noted with other abused substances as well, but LSD effects predominated over six other types of abusable substances. We conclude that LSD exerts continued effects on visual function at least 2 years following exposure to the drug.

The study of hallucinogenic drugs provides the psychological sciences with unique tools for probing aspects of mind and madness. Since the pandemic abuse of hallucinogenic drugs in the late 1960s, the drug lysergic acid diethylamide (LSD) has continued to be used recreationally in the United States, particularly among adolescents. In the decade from 1975 to 1985, for example, despite a downward trend, from 11.3 to 7.5% of 189,000 high school seniors reported using the agent at least once (Johnston, O'Malley, & Bachman, 1986).

Although a number of acute LSD studies have described a broad range of sensory disturbances (Abramson, Jarvik, & Hirsch, 1955; Abramson et al., 1955; Jarvik, Abramson, & Hirsch, 1955a, 1955b), chronic sensory studies, conducted days to years following drug exposure, have yielded conflicting results (Acord & Barker, 1973; McGlothlin, Arnold, & Freedman, 1969), in part related to ethical constraints of predrug–postdrug designs in humans. Case-controlled studies reported a variety of long-term perceptual changes in humans, including a unique syndrome of disturbances called flashbacks (Abraham, 1983; Eisner & Cohen, 1958; Horowitz, 1969); and an abnormality in a color perception test (Abraham, 1982). One controlled study (McGlothlin & Arnold, 1971) retrospectively found consistent visual differences in a group of nonmedical LSD users, compared with patients who used the drug in psychotherapy and patients with no previous drug exposure.

An acute LSD study of visual psychophysics with 19 medical students (Krill, Wieland, & Ostfeld, 1960) found changes in the physiological dark adaptation (DA) curve. Two other studies in humans found conflicting effects of the drug on the perception of critical flicker frequency (CFF) (Holliday, Hall, & Sharpley, 1965; Landis & Clausen, 1954).

Reviews of 96 acute drug-dose study combinations on the effect of a variety of agents on CFF in humans concluded that 51 out of 79 studies in which inferential statistics were used found CFF to be drug sensitive. Sedatives tended to decrease CFF responses, and stimulants tended to increase them (Smith & Misiak, 1976). Two perceptual studies in animals found long-term visual dysfunction following LSD administration (Friedman & Carey, 1978; Sharpe, Otis, & Schusterman, 1967).

Abraham (1983) described episodic visual phenomena of 123 past users of LSD selected on the basis of past drug exposure. The most common visual disturbances in this sample included geometric hallucinations, false perceptions of movement in the peripheral visual fields, trailing imagery, and positive afterimages. Symptoms were reported in some users as long as 8 years after the last use of LSD.

If LSD chronically alters the flow of impulses through the visual nervous system, one might find abnormalities in tests of CFF and DA. Accordingly, the following study was performed.

Method

The sample of LSD users in this study was recruited in response to a notice that sought "LSD users" from the Acute Psychiatric Service of the Massachusetts General Hospital in Boston. Chemical analyses of street samples of alleged LSD at the time the current study group reported drug use found the putative LSD to be verified LSD at least 93% of the time (Cheek, Newell, & Joffe, 1970). Inclusion criteria for the study were (a) a history of at least one exposure to LSD a week or more prior to testing; (b) the description of a characteristic drug response lasting for 6–12 hr, with predominantly affective and perceptual changes; and (c) reportage of using the drug in an epidemiologically likely form. Effort was made not to select for putative casualties of LSD use. Twenty-four persons were consecutively selected who fulfilled the study's inclusion criteria; of those, 20 were psychiatric outpatients, and 4 were nonpsychiatric employees of metropolitan Boston hospitals. The mean number of life LSD exposures was 46.5 ±14.1. The mean time from last LSD use was 111 weeks, with a range of 1 to 260 weeks. Seventy-two percent were male. The mean age was 22.3 ±0.8 years. All subjects were Caucasian. No subject had any central nervous system disorder related to trauma, infection, or metabolic disturbance secondary to the ingestion of other psychoactive agents in the preceding 24 hr.

This work was performed at the Departments of Psychiatry, Harvard Medical School, the Massachusetts General Hospital, and St. Elizabeth's Hospital of Boston; and the Eye Research Institute of the Retina Foundation of Boston. It was supported in part by a grant from the William R. Milton Fund of Harvard University.

We are grateful to William Anderson for his support and guidance throughout this project.

Correspondence concerning this article should be addressed to Henry David Abraham, Director of Psychiatric Research, St. Elizabeth's Hospital, 736 Cambridge Street, Boston, Massachusetts 02135.

Each subject underwent a diagnostic psychiatric interview, systematic drug history for seven classes of abused substances, and a questionnaire of demographic items and schedule of 10 visual disturbances associated with LSD: pseudohallucinations, false perceptions of movement in the peripheral visual fields, flashes of color, intensification of color, trailing of moving imagery, positive afterimages, haloes, and dysmegalopsias (Abraham, 1983).

Life use of each of seven drug classes was scored as follows: hallucinogens both by presence or absence of life exposure, and by total number of life exposures to LSD or mescaline. For marijuana, amphetamines, narcotics, sedatives, and cocaine, 0 = *no use,* 1 = *once a month or less,* 2 = *once a week or less,* 3 = *2–7 times a week,* 4 = *more than once a day.* Alcohol abuse was scored by the Ewing-Rouse CAGE criteria, a 0–4 scale of increasing difficulties with alcohol (Ewing & Rouse, 1970). No subject had used phencyclidine. The study instruments and the means of ascertaining reliable drug histories have been previously described.

To this sample was matched a control group of 20 volunteers chosen from the same clinic. Controls were matched for age, race, sex, marital and employment status, psychiatric patienthood, and history of previous psychoses. No control subject had ever used LSD or mescaline. There were no statistically significant differences between the LSD and control groups for the lifetime abuse of any drugs other than LSD, using a two-tailed Fisher's Exact Test. All testing followed the initial interviews, and was performed by the same psychophysicist (Ernst Wolf), who was protected from knowledge of the drug histories of each subject.

Psychophysical Procedures

For a comprehensive series of visual function tests a Titmus Optical Company T-O Vision tester was used, containing standard light sources and slides. Tests included visual acuity at 7 m and 0.355 m, binocularity, horizontal and vertical phorias, and color vision with six Ishihara plates. If any errors were made, further studies were carried out with a Farnsworth D-15 or 100 Hue Test.

Intraocular clarity was scored by slit lamp microscope on a scale from 0 to 5, in which 0 = *absolute clarity,* and 5 = *high turbidity.* Separate scores were made for each eye, including the cornea and lens, and vitreous (Wolf & Gardiner, 1965).

Glare

The effect of glare was measured with a glare meter (Wolf, 1965). The subject looked at a translucent screen 75 cm from the cornea, while the subject's head rested on an adjustable forehead and chin rest so that the subject's eyes were at the same level as a central glare source, subtending a visual angle of 2°, and variable in log unit steps from 0.8 to 13.000+ mL. On the screen Landolt rings were displayed 4°, 7°, and 10° from center and located on the horizontal, vertical, and oblique radii so that 3 circles of test objects were seen. Each Landolt ring had an outer diameter of 7.8 mm, an inner diameter of 4.6 mm, a width of 1.6 mm, and a width of gap of 1.6 mm. The gap subtended a visual angle of 8 min of arc for which the resolution requirement is 20/60. At low photopic luminance of the screen and in the absence of glare the gaps were easily seen. For testing, a subject was brought into the examination room with low ambient illumination, seated in front of the tester and asked whether the rings on the screen were visible, and whether the positions of the breaks under moderately high illumination were identifiable. If there were no difficulties, the lights were turned off, except for glare at the lowest level. During a 5-min dark adaptation period the test procedure was explained. When the glare light was well visible, the screen luminance, which thus far was held at subthreshold level, was raised in 0.1 log unit steps until the gaps in the rings closest to the glare source (at 4°) became perceptible and the gap positions were correctly identified. The screen luminance was recorded. The glare luminance was then raised a log unit and again the screen luminance was raised sufficiently to identify the gap positions correctly. This procedure was continued until the highest glare level was reached in five steps.

Flicker Perimetry

The study used as its test object a circular spot of light with 2° angular subtense presented at fixed positions of the visual field in each eye separately. A Sylvania glow modulator tube (R1131C) activated by a Grayson-Stadler flicker apparatus used as a square wave generator served as the flicker target. The target was held by an arm capable of being moved in a radius of 1 m to any desired position with respect to a central fixation point. The light of the test object was bluish-white. At fusion its luminance was 79.5 mL. It had a light-time:dark-time ratio of 1:1. Adaptation to dim light was achieved during a 3-min to 5-min period in which the procedure was explained to the subject. Positions progressed in 10° intervals along the horizontal and vertical meridians from the fovea to 60° in each direction. Each subject used a head and chin rest, and was asked to fixate on a central fixation mark. There was no use of an artificial pupil. Throughout testing the precision of fixation was controlled by the psychophysicist. Flicker became noticeable when its frequency was reduced slowly from 70 Hz to the critical flicker frequency. At that instant the subject responded by pushing a hand-held button of a buzzer. The CFF value was read from the dial of the square wave generator activating the glow modulator tube and entered onto a topographical field chart. Thus, a map with point for point measures of sensitivity in an extended area of each subject's visual fields was obtained (Wolf, Gaeta, & Geer, 1968; Wolf & Hirose, 1974).

Dark Adaptation

Dark adaptation measurements were recorded using a Tübinger perimeter after positioning the subject's preferred eye at the center of the perimeter's hemispheric shell while the subject fixated on a central mark. During pre-exposure, the entire visual field was evenly illuminated at 340 fL for 3 min. The test field of white light was circular, subtending a visual angle of 2°, and located 10° from the fixation point on the horizontal meridian of the nasal field. Threshold luminances were obtained by presenting the test field in the form of flashes of 0.1-s duration at intervals sufficiently long for the subject to respond, while the tester changed flash luminances repeatedly until a threshold was established. These measurements were repeated at intervals of 1.0–1.5 min until the process of adaptation indicated an approach to a final level. Subsequently the test field was shifted to other positions from 5° to 30° from the center on the nasal and temporal sides of fixation. Thus, a threshold profile was obtained.

Statistical Treatment of the Data

Mean scores for visual acuity, binocularity, horizontal and vertical phorias, color vision, and intraocular clarity were compared between the LSD and control groups by using a two-tailed Student T Test from the Statistical Analysis System package (SAS, 1985). Acuity under glare was studied using an analysis of variance (ANOVA) using the same software. The dependent variable was the quantity of light needed for correct perception of the Landolt ring orientation, with glare and LSD exposure the independent variables. The General Linear Model of the SAS system was used.

For the CFF portion of the study, an ANOVA was performed with flicker frequency as the dependent variable, and drug status and retinal location as independent variables. Retinal location was defined by using the aforementioned CFF loci. In addition, mean just noticeable flicker frequencies were plotted for each eye in both horizontal and vertical dimensions for each group.

For the DA aspect of the study, an ANOVA was also performed, with

time in the dark rounded to the nearest minute. The dependent variable was light threshold. The independent variables were time and LSD exposure. The DA curves were plotted with time in minutes on the abscissa and luminance in log millilamberts on the ordinate. The mean threshold profile for each group, performed at the end of the dark adaptation study, was likewise subjected to an ANOVA, and plotted over a range of the preferred eye from 30° on each side of the fovea in 10° increments. Subjects whose preferred eye was the left had their values rotated left for right to permit graphic plotting of the values of all patients with respect to the optic disk. For this ANOVA, the dependent variable was the light threshold, and the independent variables location on the retina and drug exposure.

To determine if there was a dose-response relation between LSD and CFF, Z scores were calculated with the mean score among controls at each retinal locus set to zero, and the standard deviation set to one. Then each data point from each LSD user was standardized against the appropriate control value. Mean Z scores for each subject's CFF and DA data were calculated with a control mean of zero and standard deviation of 1. The means were then assigned to dosage cells based on life LSD exposures as follows: zero exposures, 1–10, 11–20, 21–30, 31–40, 41–50, and > 50 life exposures. For each dosage level a grand mean CFF Z score was calculated. This procedure was then repeated for DA data.

To ascertain the relative role that other types of drug abuse played in visual function, ANOVAs were calculated using each drug class as the independent variable, and CFF and DA data as the dependent variables. In addition, a polydrug abuse model was explored, regressing the two dependent variables against all seven classes of abusable substances.

Finally, Pearson product–moment coefficients were calculated for the total number of 10 possible visual disturbances described by each subject by each of the seven classes of abusable substances.

Results

There were no significant mean differences found between groups for near and far visual acuity, in each eye separately or together. Nor were there any statistical differences between groups on testing color vision with the Ishihara and Farnsworth D-15 tests; stereo vision; ocular convergence; and corneal and lens clarity. Control subjects had a slight increase in vitreous turbidity; with zero a perfectly clear rating, the right eye for controls was 1.53, compared with LSD users' 0.80; and the left eye was 1.63, compared with 1.05 (each comparison $p < 0.05$, two-tailed). The ANOVA for acuity under glare also showed no LSD effect.

Figure 1 illustrates the CFF findings. The LSD subjects required a mean reduction of 1 to 7 Hz compared with the values of the control group before they are able to recognize flicker. This appears to be the case at every locus beyond 10°. The effect of LSD on CFF measured by the ANOVA is highly significant, $F(1, 2360) = 34.6$, $p < 0.0001$. The interaction between LSD status and stimulus location on the retina is also significant, $F(12, 2360) = 9.4$, $p < 0.0001$, suggesting a particular vulnerability to LSD within peripheral visual processors.

Figure 2 illustrates the DA (A) and threshold data (B). At every minute of the mean DA curves the LSD users require 0.64 ±0.20 log units more light to discriminate the stimulus from the background. At 10 min adaptation, for example, LSD users require 2.51 times more light than controls to see the test object. The ANOVA for the LSD effect on DA was highly significant, $F(1, 409) = 80.2$, $p < 0.0001$.

In similar fashion, the threshold profile in Figure 2B shows that the LSD group requires as much as 3.16 times additional light after 15 min for the stimulus to be perceived. Likewise, the ANOVA for drug effect is highly significant, $F(1, 193) = 99.9$, $p < 0.0001$.

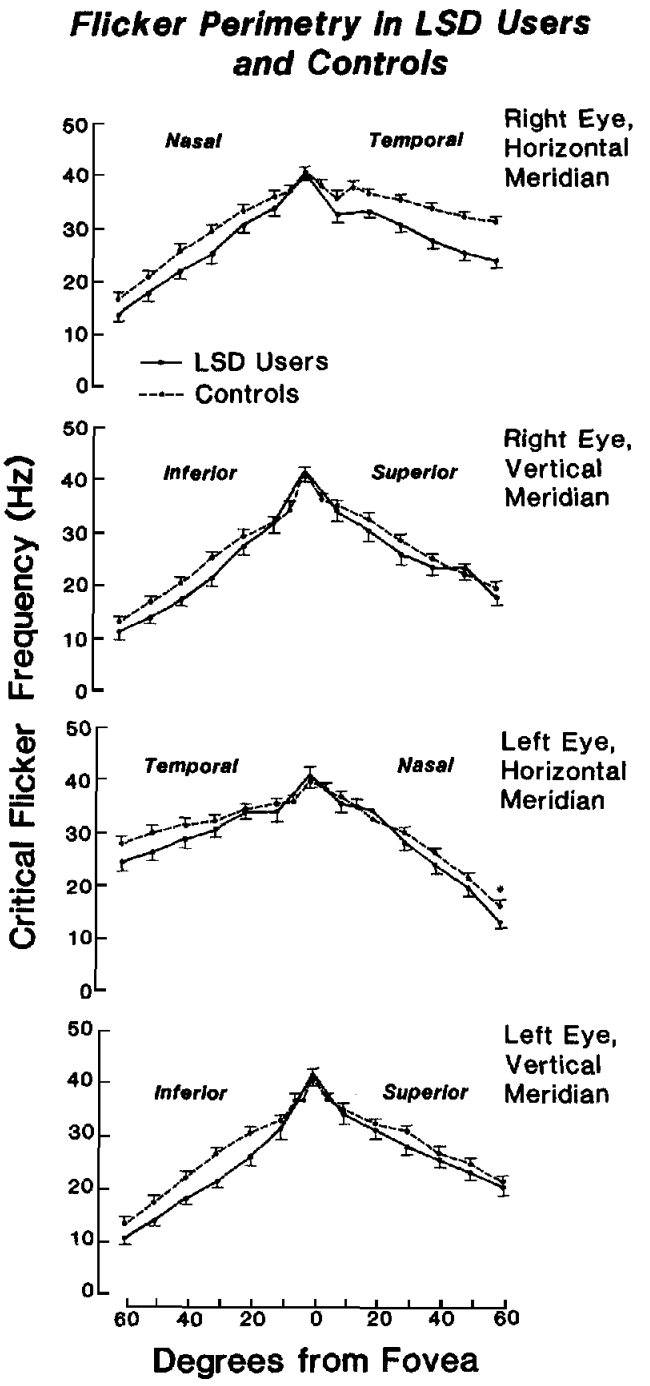

Figure 1. Bidirectional flicker perimetry, in each eye separately for past LSD users and controls. (The figure is presented from the viewpoint of the subject, so that the temporal field of the right eye is marked from 0° to 60°; the temporal field of the left eye is marked from 0° to −60°. In the vertical dimension, the superior field of each eye is denoted from 0° to −60°; the inferior field is from 0° to 60°. The notch visible at 10° of the right eye, and −10° on the left, corresponds to the location of the optic disk.)

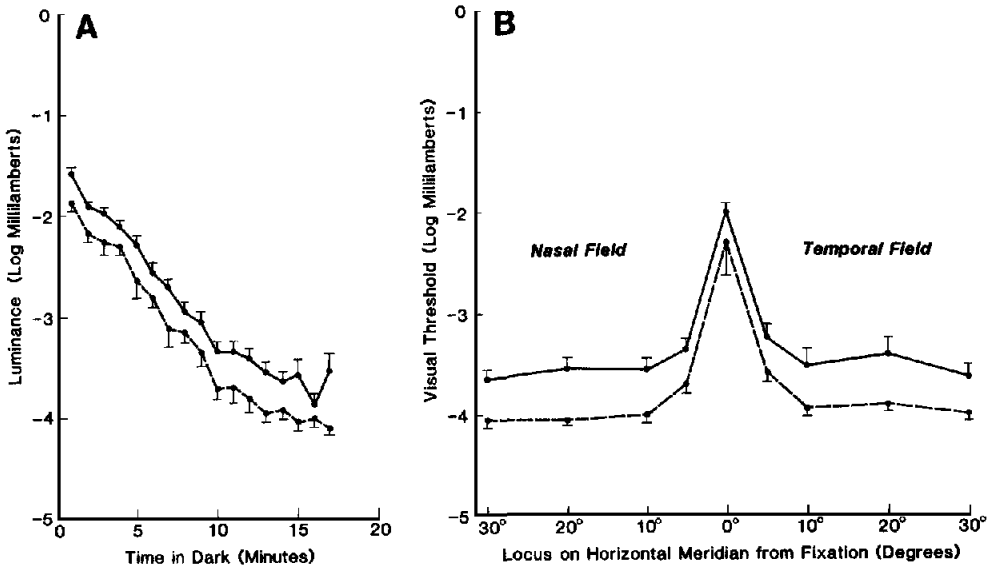

Figure 2. Dark adaptation curves for LSD users and controls (A), and visual threshold in LSD users and controls after 15-min dark adaptation (B). (The threshold response for each subject was rounded to the nearest minute, and for each minute a mean threshold ±SEM was calculated. LSD users are represented by the solid line, controls by the dashed line.)

Table 1 shows the dose-response relation between mean life LSD dose and CFF and DA responses. There is a clear-cut drug effect on both CFF and DA studies.

Table 2 shows correlation coefficients between seven classes of abusable substances and subjectively reported visual disturbances. The table also shows ANOVAs for CFF and DA data as a function of each drug class. Two drugs, LSD and marijuana, correlate with visual disturbances. Of these two, LSD shows the strongest association ($r = 0.60$, $p < 0.0001$). The other drugs generally show a declining correlation with visual disturbances as would be predicted by their respective abilities to stimulate or depress the central nervous system. For CFF there are strong effects for LSD and narcotics, with the LSD effect the greatest. ANOVA data for DA are most significant for marijuana and LSD. A polydrug abuse model for all agents' effects on CFF and DA was also significant, $F(6, 271) = 10.3$ and 4.7, respectively, $p < 0.0001$, but not as strong as the LSD effect alone.

Discussion

Taken together, these findings suggest a long-term dysfunction in the peripheral visual function of polydrug, and in particular, LSD-exposed, individuals, adding more evidence to the clinical and pharmacological hypothesis that LSD is associated with long-term changes in central nervous system function. An increase in intraocular turbidity in the control group strengthens the findings. The dose response curves for CFF and DA may reflect a strong drug effect, even at low doses; unreliable reportage; or variability in the nature of illicit LSD. It is possible that the DA differences reflect pupillary differences between the LSD users and controls.

The finding of a chronic, generalized increase in the dark adaptation threshold supports the findings of Krill et al. (1960). These workers reported an increase in the DA curve of 0.55 ±0.15 log units of light required by volunteers under the acute influence of LSD, as well as a 3-min delay in the appearance of the rod segment of the DA curve. Our past LSD users required 0.64 ±0.20 log units of light, with the suggestion of a 2-min delay in the rod portion of the DA curve, but with an abnormal elevation of both segments.

Barlow and Sparrock (1964) have proposed that a change in visual noise is responsible for all changes that occur during dark adaptation, in that preadaptation bleaching of retinal pigment predisposes receptors to become noisy by the generation of positive afterimages. Compatible with this proposal is that LSD users clinically describe the existence of trails and spontaneous positive afterimages as part of the posthallucinogen sensory disorder.

False perceptions of movement in the peripheral fields have been clinically noted in other conditions as well as post-LSD disorders, for example, paranoid schizophrenia, cocaine, and amphetamine use. Each of these conditions represents a situation of increased central nervous system arousal. Possible

Table 1
Mean Critical Flicker Frequency (CFF) and Dark Adaptation (DA) Z Scores as a Function of Life LSD Exposures

LSD exposures	CFF Z score ± SEM	DA Z score ± SEM
Controls	0 ± 1	0 ± 1
1–10	−1.07 ± 0.19	0.90 ± 0.33
11–20	−1.77 ± 0.32	1.10 ± 0.47
21–30	−0.97 ± 0.69	0.75 ± 0.29
41–50	−0.65 ± 1.42	0.95 ± 0.40
>50	−0.94 ± 0.52	1.34 ± 0.52

Table 2
Associations Between Past Substance Abuse and Measures of Visual Function

Drug class	Visual disturbances	p^a	CFF	p^b	DA	p^b
LSD	0.60	<0.0001	71.5	<0.0001	19.1	<0.0001
Marijuana	0.49	= 0.0038	6.1	0.01	19.3	<0.0001
Amphetamines	0.15	*ns*	5.5	0.02	6.3	0.01
Alcohol	0.07	*ns*	1.2	*ns*	0.3	*ns*
Narcotics	−0.14	*ns*	22.1	<0.0001	4.4	0.04
Cocaine	−0.24	*ns*	2.7	*ns*	1.7	*ns*
Hypnosedatives	−0.31	*ns*	0	*ns*	0.3	*ns*

Note. CFF = critical flicker frequency; DA = dark adaptation.
[a] The association between various drugs and subjectively reported visual disturbances was tested with Pearson correlation coefficients. [b] Values for CFF and DA are *F* statistics from analyses of variance.

mechanisms include drug-enhanced summation within the peripheral retina, behavioral sensitization, and kindling (Abraham, 1986).

References

Abraham, H. D. (1982). A chronic impairment of colour vision in users of LSD. *British Journal of Psychiatry, 140,* 518–520.

Abraham, H. D. (1983). Visual phenomenology of the LSD flashback. *Archives of General Psychiatry, 40,* 884–889.

Abraham, H. D. (1986). Do psychostimulant drugs kindle panic disorder? *American Journal of Psychiatry, 143,* 1627.

Abramson, H. A., Jarvik, M. E., & Hirsch, M. W. (1955). Lysergic acid diethylamide (LSD-25): X. Effect on reaction time to auditory and visual stimuli. *Journal of Psychology, 40,* 39–52.

Abramson, H. A., Jarvik, M. E., Kaufman, M. R., Kornetsky, C., Levine, A., & Wagner, M. (1955). Lysergic acid diethylamide (LSD-25): I. Physiological and perceptual responses. *Journal of Psychology, 39,* 3–60.

Acord, L. D., & Barker, D. D. (1973). Hallucinogenic drugs and cerebral deficit. *Journal of Nervous and Mental Disease, 156,* 281–283.

Barlow, H. B., & Sparrock, J. M. B. (1964). The role of afterimages in dark adaptation. *Science, 144,* 1309–1314.

Cheek, F. E., Newell, S., & Joffe, M. (1970). Deceptions in the illicit drug market. *Science, 167,* 1276.

Eisner B. G., & Cohen, S. (1958). Psychotherapy with lysergic acid diethylamide. *Journal of Nervous and Mental Disease, 127,* 528–539.

Ewing, J. A., & Rouse, B. A. (1970, February). *Identifying the hidden alcoholic.* Paper presented at the 29th Congress on Alcohol and Drug Dependence, Sydney, Australia.

Friedman, H., & Carey, R. J. (1978). Long-term effects of LSD-25 on easy & hard visual discrimination in rats. *Pharmacology, Biochemistry, & Behavior, 9,* 809–812.

Holliday A. R., Hall, G. M., & Sharpley, R. P. (1965). The effects of lysergic acid diethylamide: I. Critical flicker frequency. *Proceedings of the Western Pharmacology Society, 8,* 48–50.

Horowitz, M. J. (1969). Flashbacks, recurrent intrusive images after the use of LSD. American Journal of Psychiatry, 126, 565–569.

Jarvik, M. E., Abramson, H. A., & Hirsch, M. W. (1955a). Lysergic acid diethylamide (LSD-25): IV. Effect upon attention and concentration. *Journal of Psychology, 39,* 373–383.

Jarvik, M. E., Abramson, H. A., & Hirsch, M. W. (1955b). Lysergic acid diethylamide (LSD-25): VI. Effect upon recall and recognition of various stimuli. *Journal of Psychology, 39,* 443–454.

Johnston, L. D., O'Malley, P. M., & Bachman, J. G. (1986). *Drug use among American high school students, college students, and other young adults* (DHHS Pub No. ADM 86–1450). Washington, DC: U.S. Government Printing Office.

Krill, A. E., Wieland, A. M., & Ostfeld, A. M. (1960). The effect of two hallucinogenic agents on human retinal function. *Archives of Ophthalmology, 64,* 724–733.

Landis, C., & Clausen, J. (1954). Certain effects on mescaline and lysergic acid on psychological functions. *Journal of Psychology, 38,* 211–221.

McGlothlin, W. H., & Arnold, D. O. (1971). LSD revisited: A ten-year follow-up of medical LSD use. *Archives of General Psychiatry, 24,* 35–49.

McGlothlin, W. H., Arnold, D. O., & Freedman, D. X. (1969). Organicity measures following repeated LSD ingestion. *Archives of General Psychiatry, 21,* 704–709.

Sharpe, L. G., Otis, L. S., & Schusterman, R. J. (1967). Disruption of size discrimination in squirrel monkeys (Saimiri sciureus) by LSD-25. *Psychonomic Science, 7,* 103–104.

Smith, J. M., & Misiak, H. (1976). Critical flicker frequency (CFF) and drugs in normal human subjects—A review. *Psychopharmacology, 47,* 175–182.

SAS user's guide, statistics: Version 5. (1985). Cary, NC: Statistical Analysis System (SAS), Inc.

Wolf, E. (1965). Glare and age. *Archives of Ophthalmology, 64,* 502–516.

Wolf, E., Gaeta, A. M., & Geer, S. E. (1968). Critical flicker frequencies in flicker perimetry: Standards and confidence limits. *Archives of Ophthalmology, 80,* 347–351.

Wolf, E., & Gardiner, J. S. (1965). Studies on the scatter of light in the dioptric media of the eye as a basis of visual glare. *Archives of Ophthalmology, 74,* 338–345.

Wolf, E., & Hirose, T. (1970). Visual sensitivity studies in primary retinal detachment and in fellow eye. In R. C. Pruett & C. D. J. Regan (Eds.), *Retina Congress* (pp. 79–90). New York: Appleton-Century-Crofts.

Received December 4, 1987
Revision received April 1, 1988
Accepted April 1, 1988 ■