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A Chronic Impairment of Colour Vision in Users of LSD

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Summary: Forty-six users of the hallucinogen lysergic acid diethylamide were compared with 31 controls on a test of colour discrimination an average of two years after their last exposure to the drug. Controls performed better than users, and LSD users without flashbacks performed better than users with flashbacks. An analysis of variance between the three groups was significant at $P < 0.001$. This study suggests that some users of LSD may have a sustained or irreversible impairment in colour discrimination.

Horowitz (1969) has described visual disturbances in man weeks to years following the use of the hallucinogenic drug lysergic acid diethylamide (LSD), but there has been little evidence to suggest a neurophysiological mechanism to explain these phenomena. A fortuitous observation made in 1972, when there was an epidemic of LSD abuse in the United States and elsewhere, initiated a ten-year study on the long term consequences of this drug in man, of which this report is part.

The observation was that former users of LSD in a drug free state were impaired, compared with non-users, when identifying the colours of a lithograph which illustrated a 3 mm white sun surrounded by a yellow aura.

Helmholtz in 1896 had described the phenomenon of simultaneous contrast, in which a neutral test object appears to take on colour as a function of its surrounding field. The hypothesis arose, therefore, that some LSD users might be suffering from a chronic disorder in the modulation of visual information, characterized by loci within the neuroophthalmic pathway failing to extinguish, for instance, the yellow of a surrounding field after the eye had shifted attention to the white signal within the field. Such a theory of increased 'visual noise' would explain a number of chronic visual disturbances in LSD users, often called flashback phenomena, such as 'trailing', after-images, and the induction of geometric pseudo-hallucinations (Abraham, 1981).

Accordingly, the following study was done.

Method

Seventy-seven volunteers between the ages of 15 and 30 were selected consecutively from the adult psychiatric outpatient department of the Massachusetts General Hospital in Boston. All subjects had near visual acuity of 20/20 or better. The lithograph from which the original observation had been made (Griffin, 1971) was mounted under controlled illumination of 25 footcandles from eight Sylvania F20 T12 bulbs. Each subject was placed 500 centimetres from the test object and asked to describe with a single word the colour of the 'sun, and not the glow around it'. If the subject reported any colour other than white, he was asked to take a step closer and try again. The distance from the picture to the corneas was measured in centimetres when the subject first made the correct response.

Following the test, a drug history was taken from each subject. Subjects were then formed into cohorts of LSD experienced and LSD naive persons.

For the purposes of this study LSD users were persons who (1) identified using any oral agent named 'LSD', and (2) described a characteristic subsequent experience, with changes in mood and perception lasting at least six hours. Controls denied such activities. Subject selection antedated popular abuse of phencyclidine. A chemical analysis of street drugs at the time our subjects were using LSD found the likelihood of street samples actually consisting of LSD was 80.3 per cent (Marshman and Gibbons, 1970). An estimated median dose per trip was 125 micrograms (McGlothlin and Arnold, 1971). The 44 users had an average of 88 exposures to the drug and a mean interval of 2.1 years since last using it. No user had taken LSD or any other strong hallucinogen within three weeks of testing. Of the 44 LSD subjects, ten had a clinical history of LSD-related flashbacks.

Statistical analysis of the data was done with a one-way analysis of variance comparing the means and variances of each of the three groups—former users with flashbacks, former users without flashbacks and controls.

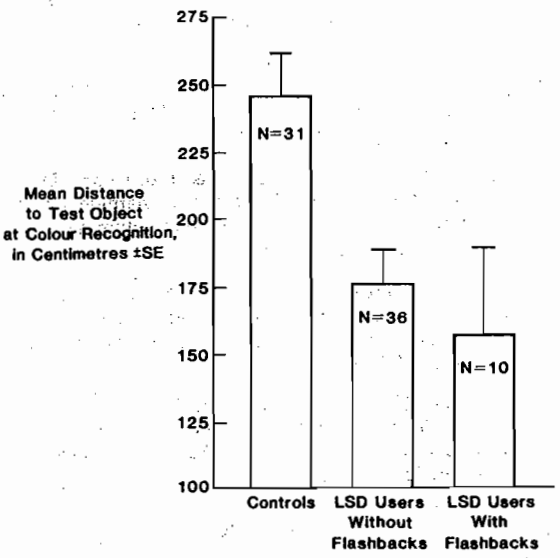

FIG 1

Results

The ten LSD users with flashbacks identified the test object's colour at a mean distance of 157 centimetres; the 34 users without flashbacks scored a mean of 176 centimetres; and the 33 controls scored highest, with a mean of 246 centimetres (see Fig 1). These differences between the three groups are statistically significant using an analysis of variance ($P < 0.001$), and significant at $P < 0.05$, using Scheffé's test, for controls versus each group of LSD users, though not between users with flashbacks and users without them.

Discussion

While our results suggest that LSD users appear to have a chronic impairment in colour perception as long as two years from the time of their last drug use, a number of caveats are in order.

Retrospective drug histories are not strong evidence of causality. There are wide variations in the illicit market (Interim Report of the Commission of Inquiry into the Non-Medical Use of Drugs, 1970). Users may be misinformed, and adulteration of drugs is common. Nevertheless, an exposure to a strong hallucinogen such as LSD is a psychologically unique experience unlikely to be confused with exposure to other agents, such as marijuana or amphetamines.

Although the test groups were matched for visual acuity, it might be hypothesized that the differences between them were attributable to the control subjects having acuity superior to the normal 20/20 while the LSD groups merely equalled it. However, at the start of testing all the subjects correctly identified the shape of the test object, a complete circle, though only a fraction correctly identified its colour.

It is suggested, instead, that the observed data are explained by an abnormal persistence of colour information within the neuroophthalmic pathway of LSD users after the primary stimulus is ended. DeValois *et al* (1958), for example, have described neurons in the lateral geniculate nucleus of the midbrain which mediate colour information by firing when monochromatic light is turned on or off. A disorder of the switching mechanism for such units might present with a continuing message; in the present instance 'yellow' when the correct message should be 'white'.

Such a hypothesis is compatible with certain biochemical findings concerning LSD in the brain. LSD is a potent antagonist to the normal action of serotonin in the peripheral nervous system (Gaddum, 1953; Woolley and Shaw, 1954). It causes an increase in brain serotonin (Freedman, 1961) and a decrease in the principle metabolite of serotonin, 5-hydroxyindole 3-acetic acid or 5-HIAA (Rosecrans *et al*, 1967). Neuronal units in the rat midbrain raphé, which have been shown to contain serotonin by histofluorescence (Dahlstrom and Fuxe, 1965), are also inhibited by LSD (Aghajanian *et al*, 1968). Similar inhibition has been shown to take place in the lateral geniculate nuclei of the baboon (Vuillon-Cacciuttolo *et al*, 1973). Serotonergic neurons have been described in the lateral geniculate nuclei (Fuxe, 1965). Finally, a competitive inhibition model between serotonin and LSD has been developed, suggesting detachment of serotonin by LSD from a hypothetical active enzyme site. This appears to be a prolonged effect, and possibly irreversible (Berridge and Prince, 1973).

References

ABRAHAM, H. D. (1981) Visual disturbances in a population of LSD users. Paper presented at the 134th annual meeting of the American Psychiatric Association, New Orleans, Louisiana, May 14.

AGHAJANIAN, G., FOOTE, W. & SHEARD, M. (1968) Lysergic acid diethylamide: sensitive neuronal units in the midbrain raphé. *Science*, **161**, 706–8.

BERRIDGE, M. J. & PRINCE, W. T. (1973) Mode of action of hallucinogenic molecules. *Nature (New Biology)*, **243**, 283–4.

DAHLSTRÖM, A. & FUXE, K. (1965) Evidence for the existence of monoamine containing neurons in the central nervous system. 1. Demonstration of monoamines in the cell bodies of brain stem neurons. *Acta Physiologica Scandinavica*, **62**, Supplement 232, 1–55.

DEVALOIS, R. L., SMITH, C. J., KITAI, S. T. *et al* (1958) Response of single cells in monkey lateral geniculate nuclei to monochromatic light. *Science*, **127**, 238–9.

FREEDMAN, D. X. (1961) Effects of LSD-25 on brain serotonin. *Journal of Pharmacological and Experimental Therapeutics*, **134**, 160–6.

FUXE, K. (1965) Evidence for the existence of monoamine neurons in the central nervous system, Part 4. *Acta Physiologica Scandinavica*, **64**, 37–85.

GADDUM, J. H. (1953) Antagonism between lysergic acid diethylamide and 5-hydroxytryptamine. *Journal of Physiology*, **121**, 15.

GRIFFIN, A. (1971) Sunrise . . . South Shore, Massachusetts. Lithograph. Copyright 33785, New England Telephone and Telegraph Company.

HELMHOLTZ, H. VON (1896) *Handbuch der Physiologischen Optik*, pp 542–3. Hamburg und Leipzig: Leopold Voss.

HOROWITZ, M. J. (1969) Flashbacks: recurrent intrusive images after the use of LSD. *American Journal of Psychiatry*, **126**, 565–9.

Interim Report of the Commission of Inquiry into the Non-Medical Use of Drugs (1970) Ottawa: Queen's Printer of Canada.

MARSHMAN, J. A. & GIBBONS, R. J. (1970) A note on the composition of illicit drugs. *Ontario Medical Review*, September, 429–41.

MCGLOTHLIN, W. & ARNOLD, D. O. (1971) LSD revisited —a ten year follow-up of medical LSD use. *Archives of General Psychiatry*, **24**, 35–49.

ROSECRANS, J. A., LOVELL, R. A. & FREEDMAN, D. X. (1967) Effects of lysergic acid diethylamide on the metabolism of brain 5-hydroxytryptamine. *Biochemical Pharmacology*, **16**, 2011–21.

VUILLON-CACCIUTTOLO, G., MELDRUM, B. S. & BALZAMO, E. (1973) Electroretinogram and afferent visual transmission in the epileptic baboon *Papio papio*. *Epilepsia*, **14**, 213–21.

WOOLLEY, D. W. & SHAW, E. (1954) A biochemical and pharmacological suggestion about certain mental disorders. *Proceedings of the National Academy of Sciences*, **40**, 228–31.

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