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An Untoward Reaction to Accidental Ingestion of LSD in a 5-Year-Old Girl

Doris H. Milman, MD

A 5-year-old girl with an apparently normal premorbid personality and adjustment became acutely psychotic following a single accidental ingestion of 100μg of *d*-lysergic acid diethylamide (LSD), with agitation, panic, depression and flattening of affect, disorientation, feelings of depersonalization, distortion of body image, and depression of intellectual functioning. In addition she displayed evidences of organic brain dysfunction: impaired visual-motor and visual-perceptual functions, and abnormality of the electroencephalogram. Within days the most florid evidences of disturbance had disappeared but the thinking disorder, distortion of body image, and depression of intelligence quotient persisted for several months. At the end of five months the only residua were the abnormal EEG and disorganization of visual-motor functions. At the end of nine months only the visual-motor functions remained impaired.

There is a growing literature concerned with the untoward effects of *d*-lysergic acid diethylamide (LSD).[1-6] The most serious complications occur as a result of self-administration by young adults.[7-9] There is also a growing body of experience with untoward reactions in carefully selected experimental subjects.[1,4,10] Information about the effect of LSD in children is sparse and, with a few exceptions,[3,9] is limited to experimental use in severely impaired juvenile psychotics.[11-14] It is of interest, therefore, to record the effects in an apparently normal 5-year-old girl of accidental ingestion of a single standard adult dose of 100μg of LSD.

Report of a Case

A white girl, aged five years four months, was admitted to Kings County Hospital on April 6, 1966, because of screaming, agitated, irrational behavior and suspicion of drug intoxication. The patient had arisen on the morning of April 6 and had begun to help herself and her younger brother to breakfast, her usual custom in that household where the adults slept late. In the refrigerator she found and ate a sugar tablet impregnated with LSD belonging to her 18-year-old uncle. Within an estimated 15 or 20 minutes the patient began to scream and cry, creating a commotion that awakened the household and alerted the uncle to the mishap. She was alternately screaming and silent. During her quiet periods she was motionless and unresponsive and apparently unaware of her surroundings.

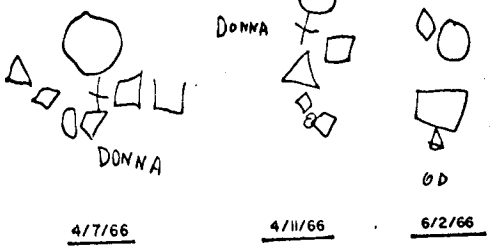
Physical examination about three hours after ingestion showed a screaming child with a temperature of 99 F (37 C), a pulse rate of 130 beats per minute, 30 respirations per minute, dilated pupils, and hyperreflexia. Treatment consisted of bed-rest and intravenous infusion of saline. Blood cell count and findings from examination of the urine were normal. The serum glutamic oxaloacetic transaminase value was elevated to 82 units and the alkaline phosphatase was elevated to 20.1 units (King-Armstrong).

After four or five hours of hospitalization with intermittent napping, the patient became relatively calm, unfrightened, and responsive. At the same time she expressed many bizarre and apparently delusional ideas, such as that her body was cut off at the waist, that she was not herself but was a girl named Dorothy (a name similar to her own, Donna), that it was not she but Dorothy who had eaten supper, that she had gone home and her bed was occupied by a girl named Dorothy. The following morning, after an uneventful night's sleep, she seemed superficially responsive and rational. However, she still maintained that Donna had gone home during the night and that she was Dorothy and she wrote her name as Dorothy. In the course of the morning she became better oriented and began to recognize that she was Donna again.

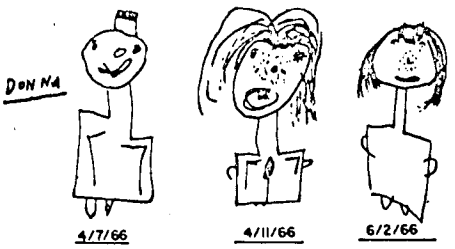
Psychiatric examination on the afternoon of April 7, about 30 hours after ingestion, showed a quiet, unreactive, apathetic girl. She responded promptly when questioned, and displayed an alertness that was in marked contrast to her prevailing apathetic mood. Her emotional range was very narrow and lacked normal modulation. Her verbalizations, although brief, were responsive and appropriate and she had a fairly good recollection of the events preceding hospitalization. In contrast to her condition of a few hours earlier, she was oriented and lucid. Her thinking was somewhat concrete. She was not able to express subjective feelings or experiences. It was inferred from her refusal to stand and her complaint that her legs "hurt" that she was experiencing either paresthesias or a residuum of the preceding day's profound distortion of body image. She described a dream in which "they stole my mommy and tried to cut her in half" which seemed to be expressing the same distortion of body image or body perception. Verbal IQ on the Ammons Quick test was 108, although it was the examiner's impression that the potential was much higher. Visual-motor performance was strikingly poor, with incoordination, impulsivity, poor planning, and poor recall (Fig 1 at top, left). Figure drawings were odd and distorted with square bodies and with arms incorporated into the trunk (Fig 2 at top, left). Findings from neurological examination were normal. An EEG showed diffuse high voltage slowing and dysrhythmia (Fig 3 at top, left).

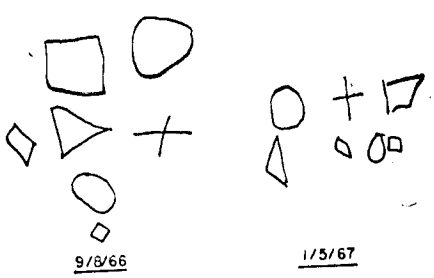
Reexamination on April 11 showed improvement in

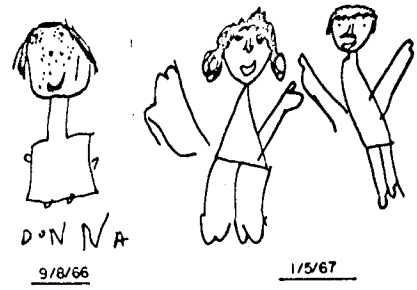
From the Department of Pediatrics, State University of New York, Downstate Medical Center, Brooklyn, New York.
Reprint requests to 450 Clarkson Ave, Brooklyn, NY 11203.



1. Geometric drawings made at serial psychiatric examinations showing incoordination, disorganization, impulsivity, poor planning, and failure to improve over a nine-month period.







2. Human figure drawings made at serial psychiatric examination over a nine-month period. The first four pictures are similarly bizarre with square bodies, stumpy extremities, elongated necks, and exaggeration of small details. The final drawings (bottom middle and bottom right) are conventional child-like renderings.

mood and a broader range of emotion. The patient was now friendly, cheerful, and flexible. Her recollections of her illness seemed to be receding and she tended to confabulate on details. Her description of her dreams was suggestive of hallucinatory experiences: ". . . saw an angel," ". . . I was seeing things, animals." The verbal content of the interview indicated some impairment of thinking processes and reasoning and some looseness of association. On the Ammons Quick test the IQ had dropped to 94. Visual motor functions were somewhat improved both in coordination and organization and control (Fig 1 at top, middle). Figure drawings were more bizarre than on previous examination, with exaggeration and distortion of minute details, eg, freckles (Fig 2 at top, middle). The EEG was still abnormal (Fig 3 at top, middle). The patient was discharged to her home on April 12.

Reexamination on June 3, two months after the accident, showed a girl whose emotional tone was appropriate in range, depth, and flexibility. Her thinking was generally relevant, logical, and coherent. She tended, however, to be overly concrete, perseverative, and circumstantial in her responses. Dream material indicated some distortion of body image, either recollected or continuing, exemplified in a dream about "chickens . . . I mean turkeys . . . some people cut off their heads while they were alive . . . then they cooked it . . . they ate it . . . they threw the bones away . . . they're not supposed to cut off their head while they are alive." Visual-motor performance was poorer than on the examination of April 11, less coordinated, and more disorganized (Fig 1 at top, right). The figure drawings were basically similar, yet somewhat less bizarre and less distorted (Fig 2 at top, right). The IQ was now 102. Findings from neurological examination were normal. The EEG remained unchanged and abnormal (Fig 3 at top, right).

Another examination was performed on Sept 8, five months after ingestion. The mother reported that the patient's adjustment and behavior after discharge from the hospital were entirely normal in all respects and in no way different from her premorbid state. (It is possible that the mother's need to establish the patient's freedom from symptoms was related to legal problems involving the uncle). The patient was found to be an essentially normal girl with normal mood, superior intelligence, and appropriate logical, flexible thinking processes. Dream material was appropriate for her age and with no unusual ideation: "a monster killing someone . . . the person died," and "someone walking in the dark and they were going to a friend's house and they were talking and then the person went home." Her IQ on the Ammons Quick test was 121, an increase of 27 over her lowest score. Her figure drawings were basically unimproved and significantly below her verbal ability (IQ equivalent, 84) (Fig 2 at bottom, left). Perceptual performance on the Wechsler intelligence scale for children (WISC) and Bender Gestalt tests showed scatter and instability. The EEG showed paroxysmal bursts of high-voltage activity and sharp wave activity over parietal and occipital leads (Fig 3 at bottom, left).

A final examination was performed on Jan 5, 1967, nine months after the incident. The patient was in first grade and reportedly progressing well. She was warm and affectionate and her mood was cheerful. She displayed some physical restlessness and fidgetiness in the examination, although she concentrated well and had a good attention span. Her thinking was logical and appropriate for her age. She was inclined to become silly when her patience was exceeded. Visual-motor performance was poor for her age, especially relative to her verbal intelligence (Fig 1 at bottom, right). Figure drawings were more conventional and age-appropriate in conception but were poorly executed (Fig 2 at bottom, right). The verbal IQ on the Ammons Quick test was 125. An EEG was now normal for the age (Fig 3 at bottom, right).

Comment

The potentialities of *d*-lysergic acid diethylamide for altering consciousness, perception, and sensation are well documented.[4,5,7,15] Untoward effects can occur with a single exposure as well as after prolonged use.[3,9,10] Among the untoward reactions are panic state, loss of judgment, paranoid states, loss of control with respect to self-injury, suicide and suicide attempts, perceptual distortions of vision and time sense, feelings of depersonalization, spontaneous recurrence of symptoms after discontinuance of use of the drug, and chronic psychosis.[3,7,9] Untoward effects appear to be more prevalent in self-administration but also occur under controlled laboratory conditions.[3,5-8,10]

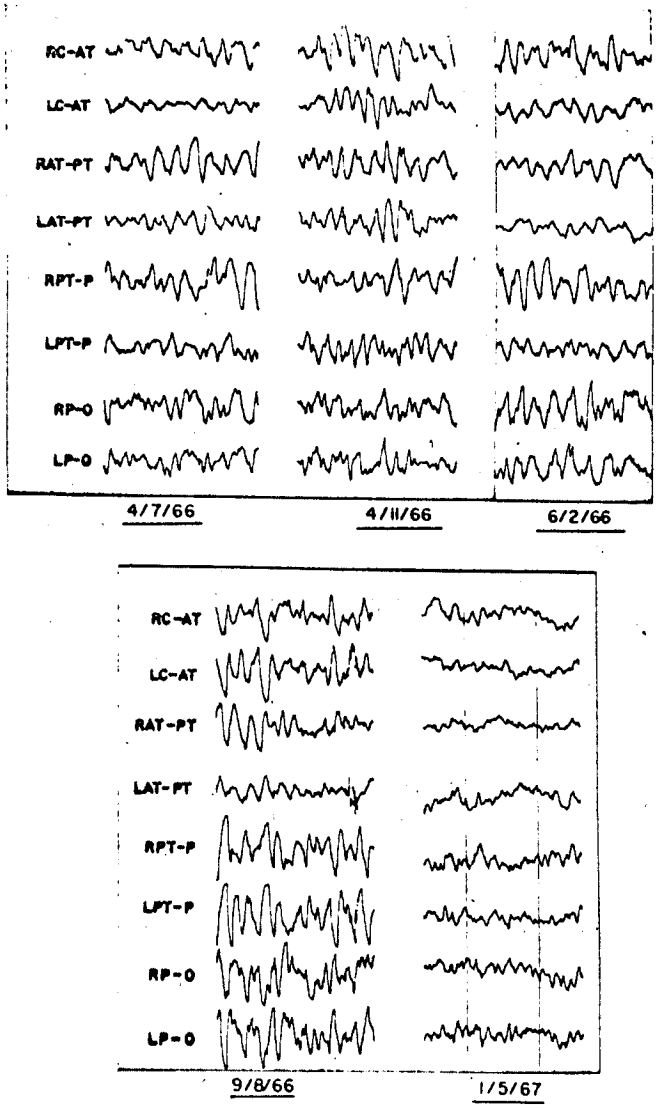
Clinical experience with children is very meager in comparison to that with adults. For the most part, observation in children has been confined to the experimental administration of LSD to children with severe psychotic disorders. The children studied

by Bender and co-workers[11] and by Freedman et al[12] were so deficient in communication that their responses could be inferred only from very gross observations of their behavior. Responses to standard doses of 50μg to 100μg administered singly or repeatedly, were neither dramatic nor clear cut nor consistent.[11-14] Bender and co-workers reported that the children they studied were happier, more spontaneous, and in a state of excitability that lasted several hours.[11] Freedman et al found lability of mood, flattened affect, auditory and visual hallucinations, increased remoteness, and, in three of the 12, catatonia.[12] Simmons et al observed no clear changes in a pair of male identical twins.[13] Rolo et al likewise found no change in a psychotic patient except for absence of hallucinations.[14] There is no report of EEG studies in these experiments or of prolonged follow-up study.

Apart from the present report, only four instances have been recorded of accidental ingestion of LSD by nonpsychotic children.[9] Three of these experienced hallucinatory reactions which, in one case, lasted for a month and required hospitalization. S. Cohen has a few additional cases in children including some in which the drug was not taken accidentally but was administered by peculiar parents (personal communication, 1966).

The present case is of interest because it involved an apparently normal child's response to a single inadvertent dose of 100μg and because of the long and detailed follow-up studies. Her reaction was strikingly similar to the usual untoward adult response, with agitation, panic, feelings of depersonalization, distortion of body image, and depression of mood. Because she was young and lacked sophistication in appreciating and verbalizing subjective responses, much of her reaction was inferred from such projective material as drawings and dreams. The figure drawings vividly illustrated the distortion of body image as well as the exaggerated visualization and enlarged perception of details.

Lacking a more subjective and introspective insight into our patient's reactions, we relied, more than other observers have done, upon objective measurements such as psychometric examinations, visual-motor performance, and electroencephalograms. The initial psychometric examination, one day after ingestion, yielded an IQ of 108. The examiner's subjective impression, based upon the patient's superior verbal facility and language usage, was that the potential intelligence was, and had been, very much higher. The drop to an IQ of 94 on the fifth day after ingestion indicated that the drug was continuing to exert a central nervous system effect even though mood and adaptive behavior were grossly normal. Even two months later the IQ was still in the same range. Four months after ingestion, with an IQ of 121, could be stated with confidence that the drug had had a clearly depressing effect upon intellectual functioning. The effects of LSD on intellectual functioning, as measured by the Wechsler-Bellevue adult scale and



3. Top, left, continuous diffuse high-voltage slow wave activity. Abnormal EEG for age. Top, middle, no significant change. Top, right, decrease in the amount of high-voltage slow wave activity. Still abnormal for age. Bottom, left, paroxysmal bursts of 5/sec high-voltage activity. Sharp wave activity over parietal and occipital leads. EEG abnormal for age. Bottom, right, normal EEG. (R signifies right; L, left; C, central; AT, anterior temporal; PT, posterior temporal; P, parietal; and O, occipital).

other tests of concentration and arithmetic performance, were studied in normal adults.[16-18] Reduced and impaired functioning was a consistent finding. There was no suggestion, as in the present case, of impairment continuing beyond the time of the immediate drug effect. However, none of the subjects was reported to have experienced a psychotic or otherwise untoward effect of the drug.

Visual-motor functions, as judged by the copying of geometric figures, were disorganized, impaired, and incoordinated, both on an absolute basis and in comparison with the child's superior verbal ability. Significantly, these functions did not improve over the period of observation, although, in response to normal maturational processes, one would have expected progressive improvement simply from

the passage of time. This observation, impairment of visual-motor coordination, has been noted in adult subjects although the implication is that it is a transient phenomenon.[15]

The electroencephalogram has been employed both in animals and in man to study the pharmacology of LSD.[10,19-21] The EEG changes appear to be in the direction of reduced electrical output, with lower voltage, decreased α activity, and a decrease in slow frequencies with an apparent but not true increase in fast activity. None of these observers carried their electrical measurements beyond five or six hours. A significant finding was that the peak of the electrical changes did not correspond in time to the peak point of concentration of drug in the body or the height of the autonomic, sympathomimetic response, but occurred one to two hours later and, in Rodin and Luby's studies, continued without subsidence up to the time of termination of the electrical studies.[10] Prolonged EEG changes lasting many weeks, associated with prolonged alterations in behavior, have been found in cats, in response to large doses of LSD (Adey, R., quoted in Cohen[9]). No prolonged studies of toxicity or brain damage in humans appear to have been done apart from the present case.

With respect to pharmacodynamics there are several theories concerning the mode of action.[10,15,21] One observation contributing to an understanding of the pharmacodynamics is that the peak of the psychological effect does not coincide in time with the most intense autonomic response. The latter occurs about 20 minutes after administration and lasts four to eight hours. Another significant observation is that, in rats, after administration of LSD, the smallest amount is found in the brain and the largest concentrations in kidney, liver, and intestine. These and other observations lead to the following hypotheses regarding mode of action: LSD may interfere with normal adrenal metabolism with resultant production of an abnormal adrenaline metabolite, or LSD or one of its degradation products may act as an antimetabolite of serotonin and cause disturbance in serotonin levels, or LSD may inhibit synaptic transmission thereby removing normal inhibitory neural processes. All of these theories presuppose that the LSD effect is not the result of interaction between the drug itself and central nervous system tissue, but rather that the drug sets off a train of secondary metabolic effects. Thus any of the above hypotheses allows for the possibility of continuance of the LSD effect for a period of time beyond the actual presence of LSD in the body. The present case offers clinical support for the existence of some sort of self-perpetuating pharmacological mechanism.

Conclusions

Several conclusions can be offered: (1) LSD can have an untoward effect, even in a single dose, and even upon a previously normal individual; (2) evidences of organic brain dysfunction are more enduring than functional psychological changes; (3) the immature brain may be more susceptible to neurotoxic effects than the mature brain; and (4) the psychological effects noted in adults can be reproduced in children and are not simply the result of suggestion or expectation.

Larry Schneck, MD, interpreted the electroencephalograms.

References

1. Cohen, S.: Lysergic Acid Diethylamide: Side Effects and Complications, *J Nerv Ment Dis* 130:30-40 (Jan) 1960.

2. Cohen, S., and Ditman, K.S.: Complications Associated With Lysergic Acid Diethylamide, *JAMA* 181:161-162 (July 14) 1962.

3. Cohen, S., and Ditman, K.S.: Prolonged Adverse Reactions to Lysergic Acid Diethylamide. *Arch Gen Psychiat* 8:475-480 (May) 1963.

4. Cole, J.O., and Katz, M.M.: The Psychotomimetic Drugs: An Overview, *JAMA* 187:758-761 (March 7) 1964.

5. Rosenthal, S.H.: Persistent Hallucinosis Following Repeated Administration of Hallucinogenic Drugs, *Amer J Psychiat* 121: 238-244 (Sept) 1964.

6. Ludwig, A.M., and Levine, J.: Patterns of Hallucinogenic Drug Abuse, *JAMA* 191:92-96 (Jan 11) 1965.

7. Frosch, W.A., Robbins, E.S., and Stern, M.: Untoward Reactions to Lysergic Acid Diethylamide (LSD) Resulting in Hospitalization, *New Eng J Med* 273:1235-1239 (Dec 2) 1965.

8. Ungerlieder, J.T.; Fisher, D.D.; and Fuller, M.: The Dangers of LSD. *JAMA* 197:389-392 (Aug 8) 1966.

9. Cohen, S.: A Classification of LSD Complications, *Psychosomatics* 7:182-186 (May-June) 1966.

10. Rodin, E., and Luby, E.: Effects of LSD-25 on the EEG and Photic Evoked Responses, *Arch Gen Psychiat* 14:435-441 (April) 1966.

11. Bender, L., Faretra, G., and Cobrinik, L.: LSD and UML Treatment of Hospitalized Disturbed Children, in Wortis, J., (ed.): *Recent Advances in Biological Psychiatry*, New York: Plenum Press, Inc. 1962, vol 5, pp 84-93.

12. Freedman, A.M.; Ebin, E.V.; and Wilson, E.A.: Autistic Schizophrenic Children: An Experiment in the Use of D-Lysergic Acid Diethylamide (LSD-25), *Arch Gen Psychiat* 6:203-213 (March) 1962.

13. Simmons, J.Q. III., et al: Modification of Autistic Behavior With LSD-25, *Amer J Psychiat* 122:1201-1211 (May) 1965.

14. Rolo, A., et al: Preliminary Method for Study of LSD With Children, *Int J Neuropsychiat* 6:552-555 (Dec) 1965.

15. Hoffer, A.: D-Lysergic Acid Diethylamide (LSD): A Review of Its Present Status, *Clin Pharmacol Ther* 6:183-255 (March-April) 1965.

16. Levine, A., et al: Lysergic Acid Diethylamide (LSD-25): XVI. The Effect on Intellectual Functioning as Measured by the Wechsler-Bellevue Intelligence Scale, *J Psychol* 40:385-395 (Oct) 1955.

17. Jarvik, M.E.; Abramson, H.A.; and Hirsch, M.W.: Lysergic Acid Diethylamide (LSD-25): IV. Effect on Attention Span and Concentration, *J Psychol* 39:373-383 (April) 1955.

18. Jarvik, M.E., et al: Lysergic Acid Diethylamide (LSD-25): VIII. Effect on Arithmetic Test Performance, *J Psychol* 39: 465-473 (April) 1955.

19. Werre, P.F.: Electroencephalographic Effects of LSD and Some Psychiatric Implications. *J Neuropsychiat* 5:516-524 (Dec) 1964.

20. Horovitz, Z.P., et al: Behavioral and Encephalographic Effects of LSD, *J Pharm Sci* 54:108-110 (Jan) 1965.

21. Pfeiffer, C.C., et al: Time-Series, Frequency Analysis, and Electrogenesis of the EEG's of Normals and Psychotics Before and After Drugs, *Amer J Psychiat* 121:1147-1155 (June) 1965.