

THE TREATMENT OF CHILDHOOD SCHIZOPHRENIA WITH LSD AND UML

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Two previous reports (4, 5) from the Children's Unit of the Creedmoor State Hospital have been made on the treatment of schizophrenic children with d-lysergic acid diethylamide (LSD-25) and a methylated derivative, 1-methyl lysergic acid butanolomide (methy-sergide-UML 491).

Starting in January 1961, we gave children, six to twelve years of age, under careful continuous observation, single doses of LSD at weekly and semi-weekly intervals and with increasing frequency, until it was evident that children could tolerate and benefit from daily doses up to 150 micrograms.

In general LSD and other psychotomimetics have been used therapeutically in a single dose at intervals of three days or more (1) to avoid tolerance. It was usually combined with psychotherapy and the desired psychotomimetic effect tends to diminish with tolerance, if the drug is re-

* Children's Unit Creedmoor State Hospital, Queens, New York. Sandoz Pharmaceuticals supplied both drugs. (LSD and UML491).

peated too frequently. The use of LSD in children has also been limited to this single-dose method (9). About 30 children so treated have been reported in the literature (4) and their acute reactions described. A subsequent change in behavior was reported in some cases.

UML, (Trade name: Sansert, Sandoz) which is less of a psychotomimetic but a more effective serotonin inhibitor has been used as a preventative for migraine and other vascular headaches on a daily basis for three years or more (12). Sixty patients under twenty years, including twelve under ten years, have been treated in this way (10).

Rationale for Treatment with LSD and UML

Our interest in these drugs was due in part to their psychotomimetic effect, hoping thereby that the autistic defenses of schizophrenic children might be broken down. Of equal interest, on a theoretical basis, is the serotonin inhibiting effect and of greater interest is their effect on the autonomic and central nervous system. Brodie (6) has described the effects of LSD and other hallucinogenic agents as "arousal and increased responsiveness to sensory stimuli, preponderance of sympathetic activity and increased skeletal muscle tone and activity." Of particular interest is their tonic effect on the vascular bed especially of the brain, as has been shown with UML in vascular headaches (8). The known effects of these drugs on perception further increases their interest in the treatment of schizophrenia (1).

Such drugs were of interest to us for the treatment of childhood schizophrenia since our definition of this condition is a disorder in maturation characterized by an embryonic primitive plasticity in all areas of integrative brain functioning from which behavior subsequently arises. This includes all autonomic functions; perception, emotion, intelligence. It was hoped that these drugs might prove somewhat specific in modifying the basic process as well as the secondary symptoms. Autism is seen as a withdrawal or denial defense against disturbing sensations arising from

disturbed autonomic function and perceptual function and anxiety in the young child with lagging and atypical maturation. It was hoped that this autism might be disrupted and that more normal autonomic functions in the vascular bed, brain, intestines, skin and other organs as well as in perception would permit more normal development.

Procedure

A preliminary report (5) was made after six weeks of daily doses of 100 micrograms of LSD and three weeks of 6 mg of UML. A second report was made a year later. This report is concerned with 54 children, six to fifteen years of age, who have received LSD or UML for two to eighteen months with an overall average of nine months. Twenty-six children received LSD and twenty-eight UML. Some effort will be made to discuss the two drugs separately though the overall clinical effects were similar.

The children were studied in the following groups:

- I. Eleven prepuberty artistic boys receiving LSD.
- II. Seven prepuberty autistic boys receiving UML.
- III. Eleven autistic (or regressed) girls, three receiving LSD, eight UML.
- IV. Eleven postpuberty "chronic" autistic boys; five receiving LSD, six UML.
- V. Twelve verbal psychotic preadolescent boys, nine on UML, three on LSD.
- VI. Two adolescent schizophrenic boys receiving LSD.

Clinical Results

I. Autistic Prepuberty Boys Treated with LSD

A group of eleven boys, now seven to eleven and a half years of age, have received daily doses of 100 to 150 micrograms of LSD daily in two divided doses, for nine to eighteen months or an average of fifteen months.

As a brief description of these children it may be pointed

out that before hospitalization all of these children had been examined by one or several professional workers in the community, and the diagnosis of autism and schizophrenia had been accepted. All these children and their parents had experienced considerable psychotherapy, and all had had some form of physiological and pharmacological therapy in the hospital. The parents of this group of children were all adequate but could not keep the children at home because of the severity of the retarded, regressed, and disturbed behavior. The children were all without any useful language; some were completely mute; some had a few words they used occasionally, and the others had psychotic, noncommunicative language. None of these children were testable with any of the standard psychological tests nor would they perform any paper-pencil tests.

At the outset of the treatment, all were removed for at least a week from the medication that they then were receiving. Blood, urine, and liver function tests were done. Blood was also drawn for biochemical studies.

A Vineland Social Maturity Scale determination was made on each child with the help of ward personnel, teachers, and mothers (Chart I). On this scale the estimated social maturity score ranged from 2-3 to 5-7 years, while their chronological ages ranged from 6-1 to 10-0 years. The range of the social maturity quotient was 32 to 60.

After six weeks the course of the children was evaluated as follows (I):

1. All tolerated the drug without side effects, toxic features, or other untoward responses.
2. All were able to get along without any other medication, although they had been accustomed to receiving other medication before the LSD was given to them.
3. All have shown some mild degree of favorable response with slow and steady progression. The amount varied from child to child. There had been no regressions although some children have had episodic recurrence of behavior familiar to them, such as feces-smearing and aggressive contact with other children.

CHART I

Prepuberty Autistic Boys

Change in social behavior as measured by Vineland Social Maturity Scale while receiving LSD

Name	Age when treatment started	Mos. on LSD and other treatment	Vineland Social Age		Gain (+) or Loss (-) in social age	Gain (+) or Loss (-) in social quotient	Diagnosis
			Beginning of treatment	Current			
	yrs.		yrs.	yrs.	yrs.		
Al.	9-1	3 mos.	1.7	2.3	+0.6	+4.1	Enceph.
Ar.	6-1	9 mos.	4.8	5.8	+1.0	+9.0	Schiz.
Cc.	6-10	10"; 3 mos. imipramine	2.8	4.0	+1.2	+7.7	Schiz.
Co	8-6	18 mos.	2.9	3.8	+0.9	+4.3	Schiz.
Gl	9-1	15"; 3 mos. imipramine	4.5	5.3	+0.9	+2.1	Schiz.
Ha	6-0	18 mos.	2.9	3.9	+1.0	+5.2	Schiz.
Sh	10-0	15 mos.; 3 mos. imipramine	4.3	5.4	+1.1	+5.6	Schiz.
Si	8-2	18 mos.	2.3	3.8	+1.5	+7.8	Schiz.
Har	8-2	15 mos.; 3 mos. imipramine; ECT	3.8	4.3	+0.5	-1.4	Organic
Ho	6-11	18 mos.	4.3	4.6	+0.3	-7.3	Devel. Defect
Wa	9-7	10 mos.; Insulin	5.7	3.8	-1.9	-30.0	Schiz.
Avg.	7-11	13½ mos.	3.6	4.2	+0.6	+3.1	

4. In general, they were happier; their mood was "high" in the hours following the ingestion of the drug, and this tended progressively to carry over through the whole day.

5. They became more spontaneously playful with balls and balloons. They participated with increasing eagerness in motor play with adults and other children if directed by adults.

6. They no longer pushed other children away or showed hostile aggression to them as much as they formerly had.

7. They sought positive contacts with adults, approaching them with face uplifted and bright eyes, and responded to fondling, affection, etc.

8. Habit patterning was improved. They handled food better and ate better. Two became toilet trained.

9. Their physical condition was improved. Their color was rosy rather than blue or pale, and they gained weight.

10. There was less stereotyped whirling and rhythmic behavior.

11. Ordinary environmental stimuli and situations were better understood and were reacted to appropriately. Thus, they responded to their own names and reacted appropriately to "yes" and "no." They fell into routine more spontaneously, and several carried out small commands. One anticipated routine and assisted in holding a door open and directing other children to the dining room.

12. The Vineland Social Maturity Scale rating was qualitatively higher in all children. A quantitative gain of one point was shown by one child, and two points by another child.

13. No children showed a recordable gain in the use of language.

After five months of receiving LSD it was interrupted with four children for three months for a crossover to reserpine 1 mg. daily, or imipramine 20-40 mg. daily, for clinical and biochemical observations. This procedure was carried out with a portion of each series of children to a total of twelve children.

At the end of a year it was reported that no child

showed evidence of side effects, toxicity or regression. All showed some type of response varying in degree and characteristics. There were definite changes in response to the environment, remarkable in these autistic children. They became gay, laughing frequently. They appeared more alert, aware, interested in watching other persons. Some showed changes in facial expression in appropriate reaction to situations for the first time. They were able to understand and follow directions more readily. This increase in awareness was noted by all observers, including families and was one of the most encouraging signs in these very withdrawn, regressed, unresponsive children. Ward personnel, teachers, parents were enthusiastic, describing the children as "more affectionate," "more aware," "more like human beings." There were no sleeping problems, though previously several had been unable to sleep without routine tranquilizing medication.

Changes in speech and verbal communication were disappointingly few. However, understanding of language improved markedly though as yet we have not been able to find an objective measure for this. Several children did increase their vocabulary if they already spoke some and their speech was more communicative. Changes in scores on the Vineland still remained minimal.

Now, after eighteen months, during which time three boys received the medication continuously and the average for all of them was nine months, more decisive results have been recorded. Of the eleven boys, eight showed striking gains measurable on the Vineland Social Maturity Scale (Chart I) and observed clinically. The diagnosis of seven was considered definitely schizophrenia. They now have a chronological age of 6-10 to 11-5 years (average 9-2). They had LSD for nine to eighteen months (average fifteen months). Their gain in social age on the Vineland Social Maturity Scale was 0.6 years to 1.2 years (average 1.1 year).

One boy Ar., the youngest (6-1 years), seemed to have improved sufficiently (eight points on Vineland S.Q. 74-80) to justify a Stanford Binet Test, but he still could not score

on this test because he would not respond to test requirements. He gained speech, naming objects, counting, singing songs, was friendly and playful.

On the other hand, the quality and extent of the improvement in these boys seemed greater than that measured by the Vineland Social Maturity Scale. They are happy, friendly, their eating and toilet habits are better. They are bright-eyed, pink in cheek and they gain weight, their sleeping habits are good. None require any other medication. They have given up stereotyped motor play, use balls, tricycles, wagons to play, adapt to school activity and routine. They understand speech and all environmental patterns. One boy has done so well in every respect except to use vocal speech, that it is difficult for us to understand why. He was given electric convulsive treatment hoping it would stimulate speech as it sometimes does in young autistic children (Bender, 1955) (2) but it was not effectual although he became more independent and self-regulating.

The eighth child (Al) that improved was a known post-encephalitic whose development had been interrupted at one year with a measles encephalitis. Although nine years of age, his social age equivalent was nineteen months. He was a crying, irritable baby who could not feed himself, swallow solid food, or make any of his wants known. Autistic defenses seemed to play a role in his behavior. After three months on LSD treatment he became cheerful, friendly, ate well, indicated toilet needs, playful and cuddly and tried to speak. Thus it would appear that this drug is favorable also in autistic children whose autism has an organic basis.

Two other boys, Ho, eight and a half years, who received LSD continuously for eighteen months, and Har, age nine and a half for fifteen months, with a three months crossover to imipramine, have shown no significant improvement on the Vineland scores, maintaining a social age equivalent to about four to four and a half years each. However, there was clinical indication of slight, variable improvement in

both of a kind that was seen in greater degree in other children. They became friendlier, sought contacts, cried less, attempted to play, had better eating habits and were enjoyed more on home visits. Similar improvement had not been observed in long periods before this.

The diagnosis in these two boys was always uncertain. Neither had a family history of schizophrenia. The home life was good and mothers were interested. One mother was toxemic in this her only pregnancy. The other child showed mild multiple congenital defects (head circumference 18½ in., simian hands, strabismus). The mother of Har. asked for electric convulsive treatment since he seemed about to improve more.

One boy (Wa) now ten years of age, was placed on LSD at eight and a half years. After six months of initial improvement, he was restless, irritable and more withdrawn. Reserpine was added without benefit, the LSD and reserpine discontinued; he was given subshock insulin treatment. He continued to regress socially, in eating, toilet habits, and independent self-care with a drop in the Vineland Social Maturity quotient from 60 to 30, speech echolalic. For a while at the age of six he had used language to communicate and could name objects. He had then been testable on Stanford Binet and Merrill-Palmer, scoring an M.A. of 2-4 (S.B.) and 2-10 (M.P.). Now at the age of ten he scores an M.A. of three years. There is no indication that the diagnosis is other than schizophrenia. The regression appears to be related to the schizophrenia and not the drug.

One might summarize by saying that autistic schizophrenic or brain-damaged children when treated with LSD are less anxious, less autistic, less plastic, tend to relate better and in general to act like more concrete, less disturbed, retarded children. The most favorable response in the youngest child is encouraging in the future selection of cases for treatment. Also the partial success achieved in non-vocal children who mature in every way, including the understanding of speech, but remain non-vocal, is a chal-

lence to find additional approaches which may still prove more successful. We still have not done all that might be done in studying changes in the autonomic nervous functions.

II. Autistic Prepuberty Boys Treated with UML

Seven autistic prepuberty boys have been treated with UML. They received one and a half space tablets twice a day, a daily dose of 12 mg. This is an accepted average dose for adults with migraine headache. They have continued the medication daily from two to fifteen months (average ten months), four had three months crossover with imipramine or reserpine.

Their age range is 7-1 to 11-9. The oldest (11-9) was also the sickest and most disturbed. His medication was carried on only two months and was discontinued more because of the mother's anxiety. His disturbed, anxious and bizarre symptoms seemed to be exaggerated during the medication while the child seemed in better contact.

The other children all improved markedly. However, UML was associated with some known side effects. One boy (age 8-3 years, with nine months of UML) had muscular spasms and vasomotor changes with episodes of cyanosis in the legs. It was his habit to sit on his crossed legs on the floor, rocking by the hour, which seemed to contribute to the unfavorable circulation in his legs and certainly made it more painful both for the child and onlooker.

Aside from this reaction, which at first was of brief duration but finally necessitated interruption of the medicine, he improved dramatically. His behavior was originally stereotyped, out of contact, a sing-song gibberish, soiling, wetting. He became able to care for himself, toilet trained, speaking meaningfully though rather narcissistic, as "Poor little Ralph, his foot hurts." Coordination improved. He understood the environment, responded to requests such as "Get off the floor. Sit on a chair." He became more of a

person. His mother was jubilant. Improvement has been maintained without further medication.

One severely regressed nine-year-old boy, who was self-mutilating, beating his head, face and nose until he had broken his nose and had cauliflower ears, improved sufficiently to stop the self-beating except for an occasional gesture when he felt frustrated. He required no other medication.

One boy of ten years has been scorable on Stanford Binet tests. At 4-6 years he scored 2-7 years; at 7-1 years he scored 4-5 years. Now at 10-3 years, he scores 4-5 years. This is after fourteen months of UML. The psychologist notes that he functions as an "essentially concrete boy" and that his principal gain has been in his ability to verbalize more appropriately and more meaningfully.

On the ward it is noted that he has improved steadily especially in speech and was able to go to a special camp for the summer and return to the ward and tell about his camp experiences. General habit patterning, i.e., feeding and dressing himself and toilet training, improved.

The general reaction of the children was the same to UML and LSD. However, there were more autonomic nervous system effects to UML, which were sometimes unfavorable. There seem to have been more leveling off of bizarre symptoms such as self-flagellation with UML, but this may have been a matter of selection of patients. There was sufficient evidence of considerable improvement at a social clinical level, with the need for more specific studies in autonomic nervous system responses.

III. Prepuberty Autistic Girls

The number of prepuberty girls referred to a children's unit like the one at Creedmoor, is always much less than the number of boys. It has been well documented (3, 11) that the incidence in prepuberty schizophrenia in girls is much

lower than in boys. It was not possible therefore to treat any equal number of young girls with a similar clinical picture as were selected amongst boys.

a) Treatment with LSD

Three girls were treated with LSD at the same time as the first group of boys. They were Bo (7-11 years), Mo (9-3 years) and Ro (7-8 years). Two received 150 micrograms of LSD daily for eighteen months. The third one (Mo) was interrupted after fourteen months of medication to receive insulin treatment, as she regressed in behavior and was losing weight (two pounds in one year). None of these three girls showed any progress in maturation or social maturity that could be scored on the Vineland Scale (see Chart II). However, two of them seemed brighter, gayer, improved in color and weight gain and eating and toilet habits. One (Bo) became too active and was aggressive with other children, and reserpine was added to her medication effectively.

b) Treatment with UML

Eight other girls, 6-1 to 9-4 years of age (average 8.2) were given UML, five receiving 12 mg. daily for twelve months to the present time. Only one of this group (Si) was considered schizophrenic. The rest were suffering from various types of organic brain disorders and congenital developmental defects. Little or no change was seen in this group of girls except that the group as a whole got along with little additional medication. Three were discontinued after two months and given reserpine and two had reserpine added to control overactivity. One girl had some muscle spasms in the legs, otherwise there were no side effects.

These results only emphasize that deviate development in girls is less common, but when it is sufficiently severe to lead to hospitalization, the girls are less amenable to treat-

CHART II
Autistic Girls

Change in social behavior as measured by Vineland Social Maturity Scale while receiving LSD or UML

Name	Age when treatment started	Mos. on LSD and other treatment	Vineland Social Age		Gain (+) or Loss (-) in social age	Gain (+) or Loss (-) in social quotient	Diagnosis
	yrs.		Beginning of treatment	Current			
Bo	7-11	18 mos. LSD; Reserpine added	yrs. 2.60	yrs. 2.7	yrs. +0.1	-5.9	Schiz.
Mo	9-3	14 mos. LSD; Insulin	1.79	1.83	+0.04	-1.7	Schiz.
Ro	7-8	18 mos. LSD	2.60	2.5	-0.1	-6.3	Schiz.
Ca	8-2	12 mos. UML Reserpine added	4.8	5.4	+0.6	-0.7	Organ. defect
Ch	6-1	2 mos. UML Reserpine added	1.83	1.89	+0.06	-2.7	Organ. defect
Ec	9-0	2 mos. UML Reserpine	5.80	5.8	0	-1.7	Organ. defect
Pa	9-4	12 mos. UML	2.90	2.9	0	-4.8	Organ. defect
Si	8-7	12 mos. UML Reserpine added	1.97	2.8	+0.73	+6.0	Schiz.
Un	9-2	2 mos. UML	3.60	3.8	+0.2	-0.3	Organic ?
We.A.	7-7	12 mos. UML Mysolin added	2.80	2.7	-0.1	-5.9	Organ. twins
We.B.	7-7	12 mos. UML	2.90	2.8	-0.1	-7.2	Organ. twins
Avg.	8-2	9 mos.	3.05	3.19	+0.89	-2.6	

ment than boys, where maturational lagging is an important feature.

IV. Chronic Autistic Postpuberty Boys

A group of eleven boys were involved in the treatment program. These were chronically ill, autistic, regressed boys twelve to fifteen years of age, who were considered more severely ill than the younger, similar group. They had been ill all their lives, had been in the Children's Unit three to six years and had not responded to any treatment method. Five were placed on LSD and six on UML, for nine to fourteen months.

Early in the treatment they showed responses similar to the young autistic children with excitability, overactivity, flushing, frequent laughing, and attempts to contact others by biting and pinching. There appeared to be an increase in their usual behavior patterns such as climbing, compulsive ball bouncing, repetitive rocking and pacing motility. One boy, who had been occasionally verbal, has shown a definite increase in verbalization and appropriate speech, dealing mostly with food and meal times. His eating habits have also improved. Fleeting attempts to contact and approach adults have been noted in some of these boys for the first time. In general, they have all shown reactions which we have come to recognize as typical responses of autistic children to these medications but to a lesser extent than the younger group. They have received reserpine for excessive biting or pinching. None of these boys were testable on standard psychometric tests, and none showed scorable improvement on the Vineland scale.

However, except for reserpine, and dilantin for one boy with occasional convulsions, none of these boys required other medication. Their sleeping pattern was good. None showed side effects from the UML. It should be emphasized that these drugs readily replace other tranquilizers

and sedatives in the ward management of a group of boys like this and do not make them groggy and sleepy as the other drugs do. Organic features such as convulsions are not contra-indications.

V. Verbal, Psychotic Preadolescent Boys

A group of twelve schizophrenic boys, eight to twelve years of age, have been on the treatment program for a year. Nine boys received UML (one and a half space tablets twice a day, a total of 12 mg.) for two to twelve months, and three boys received LSD (150 micrograms in two divided doses) three to five months. All of these boys were testable on standard psychological tests, all had attended public schools with more or less success and all were verbal and responding to the environment.

They showed considerable pathology in behavior. Some were clinging and dependent on adults while avoiding their peers with whom they could not identify. Some were negative, hostile, aggressive, moody, anxious. They described terrifying dreams and anxious fantasies. They were especially preoccupied with body image disturbances, flying or space fantasies, death threats to themselves or parents, introjected voices, identification confusion. Most of the boys showed irregular or sighing respiration, rapid irregular pulse, pallor with blue lips, moist hands, whirling on the longitudinal axis in response to the neck-righting postural test.

These boys had been on other medication which was discontinued a week before the UML or LSD was started. When they received a phenothiazine, they were often sleepy, especially in the afternoon in school. They were never sleepy with UML or LSD and expressed preference for these drugs for this reason. None of them was ever a management problem requiring additional medication. They slept normally at night.

None of these boys received psychotherapy with the

medication, although all had interviews at intervals by the authors. Their school and activity program continued as usual, with reports from teachers.

Where parents were available, the boys made their usual weekend and holiday visits at home.

Six boys were discharged to the families on convalescent care. Four of these with cooperative families improved steadily reporting to us for after care and making adequate school adjustments although one was in a low IQ class. Two returned to the hospital due more to the inadequacy of a single parent (mother) than to the boys' faults.

Dramatic changes were noted in the handling of fantasy material in interviews during the period of medication. Bizarre fantasies experienced in the first interview were explained by saying, "I was sick then" or "I was acting crazy like a cartoon"; or the fantasies were experienced only in nocturnal dreams or accounted for as derived from the television or comic books and science fiction. Paranoid attitudes found expression in reality situations such as abuse from other patients or neglect by parents, anxiety and depression explained by their hospitalization and real family problems. Body sensations were described as hypochondriacal complaints rather than bizarre body image distortions. Introjected voices and objects were no longer experienced. They appeared to have developed rationalized or denial defenses with considerable insight of an adult type.

We discontinued one boy (Wm.) where depression with a paroxysmal EEG dominated the picture, although a marked improvement occurred in intellectual organization and motivation with an eight point rise in IQ. On benzedrine for six months, the IQ fell off six points in performance, the boy was less depressed but more irritable.

Of the twelve boys in this group, about half received two psychological examinations,* the first when the LSD

* The report on psychological studies was prepared by Leonard Cobrinik, Ph.D., Senior Psychologist for the Children's Unit, Creedmoor State Hospital.

and UML program was started, the second three months later. The remainder of the group had a third examination approximately six months after institution of the program. The test battery consisted of the Rorschach Test, the Human Figure drawing, and the Bender-Gestalt test, and educational achievement tests. Recently, we have reexamined children still available to us with a more complete battery of psychological tests including the Wechsler Intelligence Scale for Children (WISC). This present testing follows the initial repeat examination by about one year (See Chart III).

Analysis of the changes which occurred between the several examinations indicated considerable variability within the group. Four boys (Br., Ha., Pi., Sh.) demonstrated noticeable or marked shift in Rorschach response between original and repeat examinations. Of this group three children show similar patterns of change consisting of

- 1) a decrease in personalized thinking and in responses expressive of morbid body preoccupation;
- 2) an inhibition of uncontrolled color responses such as "fire" and "blood";
- 3) improved accuracy of perception and gradual development of human figure percepts.

One child (Pi) in this group demonstrated decreased fluidity in thinking as well as a decrease in color description type of response. However, in this child, there was some evidence of a shift from immature types of reaction (confabulations, dark shading reactions) to more deviant, individualized responses.

Three of the children (Sh, Ha, Br.) who showed improvement in Rorschach response, were among those recently reexamined. Two of these children demonstrated substantial gain in WISC IQ (thirteen and nine points in full scale IQs). While the gains were noted in both verbal and performance areas, they were more marked on the latter, and an analysis of subtest patterns indicated that the gains were not simply practice effect. (All three children, for example, demonstrated marked gain on the picture comple-

CHART III
Psychological Studies on Verbal Psychotic Prepuberty Boys

Name	Age ¹	Drug ²	WISC ³		Reading ⁴	
			1st	2nd	1st	2nd
An	9-10	2 mos. UML	88	104		
Han	10-11	11 mos. UML	93	102	2.9	6.0
Haz	10-6	5 mos. UML	83	96	1.6	1.8
He	11-0	6 mos. UML	69	66	2.5	3.3
Pe	10-0	4 mos. UML	79	1.6
Pi	9-6	6 mos. UML	61	59	0	0
Ro	11-2	12 mos. UML	114	110	4.7	6.5

1. Age—at onset of drug treatment.
2. Drug—Time in months of daily drug treatment.
3. WISC—Full score 1st—when drug treatment started; 2nd—currently.
4. Reading grade achievement level. 1st. 2nd as for WISC.

Rorschach ¹	Drawing ²	Clinical Comment ³
1 R. Thought disturbances. Excess fantasies. Personalized egocentric responses.		Schiz. and ⁴ migraine type headache. EEG foci. Clinical improvement.
2 R's. 2nd more efficient. Simple, popular responses.	2nd gestalt less fluid. More control. "Man" less primitive.	Intellectually more efficient. Paranoid and hostile. Changed to thorazine—sleepy.
3 R's with greater productivity, more accurate perception, less body preoccupation. More color response.	Gestalt more disorganized. Man - immature.	Body image fantasies, hallucinations, improved. Went home, returned with acting out. self-mutilation.
3 R's. No change. All showed immaturity, impulsivity, poor boundaries.	Gestalt better control, rotation. Man - more mature, better detail.	Organic factors (?) Inadequate. No progress in maturation. Basically defective.
3 R's basically same. Anxious, immature.	Gestalt more stable, less rotation. Man improved, crude "Superman."	Remission. Home and school (spec. class) and after care.
3 R's. Shift from shading and from confabulation. Less color reaction. Less fluidity.	Gestalt same. Man more primitive.	Less disturbed. Home—in dependent role. Inadequate, defective.
3 R's. Identical except less use of pure color and color descriptions.	Gestalt same. Man same.	Remission. Withdraws into reading. Explains fantasies by reading material, comics, science fiction, etc.

5. Rorschach—Number of Rorschachs administered and comparison of results.

6. Drawings. Bender gestalt test called "gestalt" and human figure drawing called "man." Comparisons of last drawings with earlier ones.

7. Clinical Comment. Pertinent notes to identify problem and general response to treatment.

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Sh	8-2	10 mos. UML	96	105	1.7	2.5
Wm	9-0	5 mos. UML	78	86	1.4	1.7
Br	9-8	5 mos. LSD	88	88	2.7	3.1
Fe	12-1	5 mos. LSD	68	72	7.3	7.0
Ha	10-1	3 mos. LSD	102	2.8

tion test, a test which may require visual alertness). At the same time it should be noted that there was some regression in quality of Rorschach response, but not to the level of the initial examination.

If it is possible to generalize from the small number of children in this phase of the study, the following statements may be made:

1) improvements were noted in children who were initially characterized by average, or near average intelligence, strong feeling (color) reactions, and the presence of individualized thinking and fantasy. Paradoxically, it appeared that it was in the area of thinking disorder that improvement was most marked.

2) such changes as were noted occurred early in the treatment program, that is, within the three month period from institution of the study to the initial repeat examination.

3) most of the gains were maintained over the longer

3 R's. 2nd decrease in personalized ideas. Human figure perception. Less pure color response. 3rd slight regression.	Gestalt same. Man slightly improved. 3rd Man — slight regression.	Tends to insightful remissions with regressive periods because of no home.
3 R's almost identical.	Gestalt variable. 4th best organized and controlled. Man primitive, unchanged.	Depressed. Paroxysmal EEG. General improvement. Drug changed to benzedrine —became irritable.
3 R's. Decreased personalized element and body preoccupations. Inhibition pure color. Better perception.	Gestalt and man—no change.	Remission. Home with steady improvement in community and school.
3 R's. All alike, simple, unoriginal, rigid responses.	Gestalt immature. Man, primitive Superman.	Partial remission. Fantasies explained by dreams. Tried to stay awake.
2 R's—all alike.	Gestalt same. Rotation. Man — better proportioned head.	Remission — home. Progressive improvement.

period (now about one and a half years), although there may be some fluctuation in general level of response.

In two other children (He, Wm.) we fail to note significant changes on any of the tests, with the exception of the human figure drawings. The changes were, however, marked in degree. Whereas the initial productions made use of crude oval forms, were drawn full face, and demonstrated a great deal of anxiety in line quality, the later efforts demonstrated greater maturity and control. Both children, however, gave meager, repetitious responses to the Rorschach. WISC results also indicated some limitation in endowment. While it is difficult to interpret the meaning of these changes, the almost spectacular nature of such change merits further study.

SUMMARY: This group of boys showed considerable and consistent effects from medication with UML or LSD daily for two to eleven months. Their behavior, ward man-

agement, school-room adjustment and progress at home changed favorably with less acting out and less disturbed behavior. They not only needed no other tranquilizing, sedative, or antidepressant medication, but furthermore, unlike the tranquilizers which made them sleepy and groggy, they were generally cheerful and alert. Personnel and families noted the difference. Repeated psychiatric interviews revealed a change in fantasy material which was less bizarre, personalized or disturbing. Depressive, anxious and paranoid attitudes were focused on real objective problems. Insight was impressive. Intellectual changes, as seen in psychometric tests, indicated improved maturity, better organization and motivation with a rise in IQ which was reflected in improved school work. The Rorschach and drawing tests also showed increased maturity and control with clearer thinking. Studies of the autonomic functions were not made.

VI. Adolescent Schizophrenic Boys Treated with LSD

Two adolescent schizophrenic boys, ages fourteen and a half and fifteen and a half, received LSD for two and three and a half months. An initial dose of 100 micrograms i.m. was given while the boys were carefully observed. Their reaction was different from all the other prepuberty children or the postpuberty autistic children, but similar to reactions of adults described in the literature (3).

They became restless, giggling, anxious and labile, licking their lips. They looked at the examiners with distrust, saying we were playing tricks on them. They felt light inside, "no weight," "my arms feel different, too big." They tried to control themselves. They tried to play cards and draw. They gave up both endeavors. Drawing of the human figure became more primitive and fragmented. They spoke of perceptual experiences. A pencil looked like rubber. There were too many lines in the corduroy of their slacks. The other boy's lips looked funny, moving and green. Dirty lines on

the walls were moving. Two hours seemed like fifteen minutes. They said, "You are cheating us out of time. You are trying to make us crazy, make us sad, make us do things." They tended to identify with each other against the examiners. Later one said, "You were making us see green ~~monsters~~ but we wouldn't tell you."

Nevertheless, they continued to take the medication orally in 75 microgram doses twice daily. These bizarre features were not mentioned again. The fourteen and a half year old showed gradual behavioral improvement and went home to his family in two months and has since made an adequate home and school adjustment.

The fifteen and a half year old has no family and has failed in many foster home adjustments. He was on the LSD for three and a half months. He was reported to be more outgoing and active but obnoxious in the schoolroom. It was discontinued because he complained that it was an experimental drug and would spoil his chances for getting out of the hospital.

It is realized that many of these observations are more impressionistic than definitive, but they do suggest the direction which subsequent studies should take indicating that LSD and UML, when given in these doses, can be tolerated daily for long periods with positive effects in general and some very specific ones.

Biochemical Studies

Two types of biochemical studies were made on these children: one on the effect of the LSD and UML on blood inorganic phosphates, and the other on the effect of the drugs on the level and uptake of serotonin and histamine.

The children who were to receive LSD or UML were withdrawn from all medication for at least a week before they were started on the LSD or UML. Blood was always drawn in the morning before breakfast. The blood drawn before the start of medication served as a pre-drug

control level. The blood was drawn at the end of the first, third, fourth, fifth and sixth week during the period of medication.

The same group of children were used to study the effects of reserpine and imipramine in a crossover study. For this purpose, the children were withdrawn from LSD or UML for a period of one month and then started on reserpine or imipramine.

In this study it was found that only LSD and UML increased the erythrocyte inorganic phosphate level significantly. Reserpine and imipramine in six children each, had no such effect. The increase in erythrocyte inorganic phosphates may be due to several factors. Some may be cited: 1) Decrease in oxidative phosphorylation; 2) Increase in phosphatase and ATP-ase activity; 3) Altered adrenocortical activity; and 4) Acidosis induced by metabolic factors. These are under further study.

The effect of a given single dose of LSD (100 micrograms) both at the beginning and in the course of therapy over a few weeks was studied. The children who reacted with a rise in erythrocyte inorganic phosphates within one hour of the administration of LSD were investigated and it was found a single dose of LSD is less effective later in the period of study than in the beginning. While approximately 70% of the children showed an increase in the red blood cell (RBC) inorganic phosphate at the beginning of the study, only 29% showed an increase later. This may indicate tolerance to or decreased effectiveness of a given single dose of LSD in the later phase.

Sankar et al (14) have shown that the uptake of labeled serotonin by blood platelets from autistic schizophrenic children (in the Creedmoor State Hospital Children's Unit) was lower than that from non-schizophrenic hospitalized children. The blood content of serotonin was shown to be higher in autistic children by Schain and Freedman (15). This may also be due to a low metabolic rate of serotonin in these children.

From the present studies on these children it was found

that both LSD and UML increased the blood level of serotonin through the period of study. In almost every case the level of serotonin was higher after a week than before the administration of the drug. The increase persisted till the end of the study (23 days). In a previous study (13) a similar increase of blood serotonin levels and not in histamine (7) levels was found by us in the rabbit fifteen minutes after the administration of 500 micrograms of LSD. These results and the higher specific activity of serotonin in rabbits given LSD after pre-treatment with radioactive 5-HTP, support the view that the administration of LSD enhances the rate of metabolism of serotonin. With the crossover to reserpine, the serotonin level was lowered.

The blood level of histamine was elevated by UML but not by LSD, thus differentiating between these two drugs. Further studies are in progress about this differential effect of LSD and UML.

The administration of LSD and UML increased the platelet uptake of serotonin in these children over the first few weeks, after which it decreased to a lower level. This raises questions about the metabolic rate of serotonin, the saturation point of platelets, which may also be related to slowing down of the effective behavioral response in the autistic children after an initial spurt of level improvement.

Summary

Reports of the treatment of disturbed children with LSD have been limited to about thirty children who received single doses at intervals of several days, with change in behavior noted in some cases.

This paper is the third report on a group of children at the Creedmoor State Hospital Children's Unit, who have been treated with LSD or UML on a daily basis.

Fifty-four patients, ages six to fifteen, have received LSD or UML daily from two to eighteen months (average nine months), with the usual dosage of LSD 150 micrograms

daily, or UML 12 mg. daily. The patients are boys and girls in the following groups: prepuberty autistic boys, autistic girls; postpuberty, "chronic" autistic boys; verbal psychotic pre- and post-puberty boys. The children were evaluated before, during, and after treatment, by clinical interviews, psychological tests, and biochemical studies, as well as routine reports and observations.

It was hoped that these drugs might prove effective in breaking through autistic defenses, improving autonomic nervous system functioning, and modifying distorted perceptual experiences.

There were some differences in results in the various groups. In general, the younger autistic children became less anxious, less autistic and plastic, more aware and responsive, with some changes in verbalization and qualitative improvement, on the Vineland Social Maturity Scale. The girls and older autistic boys showed similar results, but much less marked and persistent. Verbal children showed improvement in general behavior, with marked changes in fantasy and bizarre ideation to more insightful, reality-oriented, though often anxious and depressive attitudes, and improved maturity and organization.

There were no major side effects, though a few patients on UML had muscular spasms and vasomotor changes in the legs, generally of a temporary nature. It is significant to note that while most of these patients had required tranquilizing or other medications, they could all now be maintained only on the LSD or UML. A few patients received reserpine to control excessive activity, aggression, or biting.

Biochemical studies in these patients showed increase of RBC inorganic phosphate level and increase of serotonin level.

Discussion

DR. CARL BREITNER (Phoenix, Arizona): I would like to inquire about the dosage used with these children. Also, I understand from your paper, Dr. Bender, that in this

study you are not using LSD the way the analytic group in California is using it, namely, to facilitate communication, but as a psychotropic drug. Do I understand you right? Then the question comes up in my mind: in what way do these schizophrenic children differ from the older group, from the adults? Because in those, usually LSD would seem to be contraindicated as a drug. As a psychoanalytic tool that is different.

DR. BENDER: We do not use it as a psychoanalytic tool. Our idea was to give it as a daily drug. It is our general experience that frequently the children respond to many drugs that affect the central nervous system differently than adults. This is common knowledge; at least, to those of us using drugs with children. So we were not surprised to find, in our early initial studies, that if the children were near puberty or in puberty they responded to the first dose with anxiety and disturbance, just as the adolescent boys did. But even these children could be maintained on high doses of the drug, just as the adolescent boys were, so that the drugs can be given to these children in continuing doses. What tolerance means, I don't know. Tolerance may be established in our patients. The chemical studies suggest this, and even our psychological studies indicate a slight change later on, a leveling off of response as compared to initial reaction, but the long-term reaction is still the most valuable reaction to the drug.

DR. ELKES: The strange and paradoxical effects of drugs in relation to maturation, quite apart from relation to endocrine, may also seem to be related to differences in the blood-brain barrier. The study comes to mind by Bradley and Morelli who have shown that in the developing rat the effect of amphetamine, for example, in certain early stages produces a sleeplike effect, whereas in guinea pigs the effect is always on the adult. Is there any consideration at all on the blood-brain barrier?

DR. BENDER: I know of no research work with LSD and the blood-brain barrier. Encephalitis affects the individual differently at different ages. If it occurs under two, the child may develop defectively and have convulsions; between two and twelve the impulse and behavior disorders of the brain

damaged child occur. After twelve, progressive Parkinsonism may develop.

DR. KALINOWSKI: I would like to underline some of the statements made by Dr. Freyhan. One is that we are still in need of all treatments available. Second, the fact that in many cases life-long remissions were not obtained with the older treatments is no argument against their value. In only partially improved patients we can now continue treatment with the newer drug methods and stabilize the improvement. A most important point made by Freyhan is the emphasis on psychopathological observations which are badly neglected at the present time. It is quite interesting that the Russian psychiatrists who are here, and with whom I have discussed some of these things, also point out the importance of coming back to clearer formulations of syndromes and of psychopathological studies. We have to come back to that if we want to make any progress, and we must also realize the importance of classification in mental illness, classification which looks for changes and progress based on our new therapeutic experience. I consider it a most important contribution when Martin Roth expressed extremely well how we can evaluate treatments only when we come to some new formulations which in this case means new formulations of syndromes, and perhaps substitute new psychopathological syndromes for the old disease entities which we now use exclusively and which, I admit, are not satisfactory.

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