COMPARISON OF TWO DRUGS WITH PSYCHOTOMIMETIC EFFECTS (LSD AND DITRAN)

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Ditran[2] is one of the more recently introduced psychotomimetic agents. In common with all other drugs in this group, it has been claimed to reproduce important aspects of naturally occurring schizophrenia (4), although Meduna and Abood (1, 13) clearly described and designated the Ditran-induced state as a delirium. It is an anticholinergic agent, and its effects are counteracted by tetrahydroaminacrin (THA), a compound with marked anticholinesterase activity which exerts central effects (5, 6). Ditran has also been reported to have a therapeutic action in various psychiatric syndromes (3, 4, 13).

The present study was carried out mainly to compare the effects of Ditran and lysergic acid diethylamide (LSD) on two quantifiable behavioral tests. These are the Bender-Gestalt (2) and Draw-a-Person (7) tests, which have previously been shown to be sensitive to LSD (15). The study was also designed to obtain objective data concerning the antidotal effects of THA for Ditran and of sodium succinate for LSD (6). In addition to the behavioral tests, Jarvik's Questionnaire (9) was administered and clinical observations were systematically recorded.

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[2] Piperidyl benzilate (JB329, Lakeside Laboratories). Each 15 mg Ditran consists of 10.5 mg of N-ethyl-1-pyrrolidylmethylphenylcyclopentyl glycolate hydrochloride and 4.5 mg of N-ethyl-3-piperidylphenylcyclopentyl glycolate hydrochloride.

There appears to have been no previous systematic comparison of LSD and Ditran in nonpsychotic subjects. Gershon and Olariu (6) administered several psychotomimetics to nine subjects, but five of these were schizophrenic and test data were not reported. Lebovits *et al.* (10–12) carried out a careful comparison of LSD and JB318 (a congener of Ditran), but their observations did not involve quantifiable performance tests. Hollister *et al.* (8) compared Ditran with psilocybin, which resembles LSD in its effects, and with IT-290 (dl-alpha-methyltryptamine), the indole analogue of amphetamine. Their observations included psychometric tests involving arithmetic and line drawing; they reported, without presenting numerical data, that both Ditran and psilocybin impaired performance on these tests, the former to a greater extent.

Beyond providing a comparative description of changes produced by Ditran and LSD, it was expected that the data would have some bearing on the question of individual susceptibility to psychotomimetic drug effects. Are some persons more susceptible than others to any psychotomimetic agent, or is the nature of the agent the main factor in determining the reaction? Gershon and Olariu (6) might have obtained data relevant to this issue, but their comparative results were reported only in terms of incidence of symptoms, and did not deal with individual susceptibility to specific symptoms. Such data on symptoms would, in any event, be difficult to interpret, as the qualitative effects of LSD and Ditran appear to differ. It seemed that valid comparisons of susceptibility might be more readily obtained by the use of quantifiable performance measures.

METHODS

Subjects: Eleven patients (of whom ten were in-patients) at the Iowa State Psychopathic Hospital served as subjects. Criteria for selection were availability; willingness to cooperate; and absence of psychotic symptomatology, evidence of brain syndrome, mental deficiency, or obvious physical disease. There were six women and five men, ranging in age from 17 to 40 with a mean of 28.4 years. Psychiatric diagnoses included three cases of psychoneurosis (recovered dissociative reactions, two; anxiety reaction, one), seven personality disorders (emotionally unstable, three; sociopathic, two; passive-aggressive, two) and one case classified as adjustment reaction of adolescence. Any medications being received were discontinued for the 48-hour period prior to testing. The procedure was explained to the individual patient by his own physician as an investigation of the effects of two medications and drugs which counteracted them. They were told that some patients might benefit from these drugs, but that the effects were variable. There was no evidence that the subjects knew the identity of the drugs used and little evidence of communication between subjects concerning the effects.

Drug administration: All procedures were carried out in the same room with the investigator and one hospital attendant present. LSD was given intravenously, diluted with water to a standard quantity of solution containing 2 mcg/kg body weight. This dose was selected as likely to produce a definite reaction in most subjects (15). Ditran was administered intramuscularly in a dose of 0.1 mg/kg body weight. Following LSD, sodium succinate was given intravenously in the amount of 15 grams in 50 cc sterile water; the injection was given slowly, requiring up to 30 minutes for administration. The slow rate was necessitated by intense flushing and marked discomfort in most subjects. Only six subjects received the sodium succinate, this part of the investigation being discontinued because of the associated discomfort. THA was given intravenously following Ditran, the dose being 30 mg in 10 cc solution; it was given over a five to ten minute interval. No untoward effects were noted after THA. The order of administration of Ditran and LSD was alternated between subjects. Time between procedures ranged from two to seven days.

Observations: The test battery was first administered prior to drug injection. Testing was commenced for the second time 30 minutes after injection of LSD or Ditran.[3] After completion of the tests, the antidote was administered. One hour after the antidote had been administered, the test battery was again repeated. Clinical observation was continuous, with the subject constantly being engaged in conversation. Examination procedures were administered in the following order: 1) Jarvik's Questionnaire; 2) formal mental status evaluation; 3) Bender-Gestalt; 4) Draw-a-Person; 5) physical examination. Jarvik's questionnaire consists of 59 items involving frequent symptoms of the LSD state; it was felt of interest to determine to what extent Ditran would affect the responses to these questions. The questions were read to the subjects and they were instructed to reply to each item with "yes" or "no." The number of positive responses constituted the score. The psychiatric mental status examination was designed to evaluate the subject's memory, orientation, calculation ability, thought processes, mood and affect. In classifying reactions as psychotic or otherwise, the criteria used in the study by Pauk and Shagass (15) were applied. These criteria require definite evidence of psychotic symptoms, *e.g.*, hallucinations must involve "re-

[3] It is recognized that the full effect of the drugs may have required longer than 30 minutes to develop. This time interval was selected mainly to restrict the duration of the experimental session, which usually lasted four to five hours. It is possible that the Jarvik Questionnaire results were affected by the early start.

ality-like" projection into the surrounding environment, and illusions are not accepted.

Bender-Gestalt Test: This test requires the subject to copy nine designs (2). Performance was scored according to the method described by Pascal and Suttell (14), higher scores indicating poor performance. The scorer standardized his method, using the sample tests in the Pascal and Suttell manual, and attained a high level of agreement with the authors' scores. Raw scores were converted to standard "Z"-scores.

Draw-a-Person Test: The subject was requested to "draw a picture of a person and make it as complete as you can." The tests were scored according to the Goodenough outline (7), after the scorer had standardized his criteria by practicing with the test drawings in Goodenough's book. Raw scores were used for analysis; a high score by this scheme indicates a higher level of intellectual performance.

Statistical evaluation: The "t" test (two-tailed) was used to determine significance of differences between means. The rank order method was used for determining correlation, with the .05 level of confidence accepted as significant.

RESULTS

CLINICAL OBSERVATIONS

The changes produced by LSD and Ditran differed markedly from one another. All subjects displayed clear psychotic symptoms within one hour after Ditran was administered, whereas only six were considered to develop a psychotic reaction with LSD. With Ditran, "toxic-organic" symptoms were prominent in every case; there was impairment in all areas of the sensorium. In addition, hallucinations were reported by five subjects, delusions were found in two, and catatonic-like mutism was noted in three. All six subjects who were considered to develop a psychotic reaction with LSD experienced hallucinations. In addition, "toxic-organic" symptoms of minimal degree were observed in four cases, and delusions occurred as well in two of these four. Illusions were reported by all subjects with both drugs, except for two with Ditran; this may have been due to their inability to communicate under the influence of Ditran. Illusions during Ditran were less colorful, less pleasurable, less fantastic and involved a minimum of motion in comparison with those during LSD.

Of the six subjects who developed hallucinations with LSD, only three were judged to experience hallucinations with Ditran. Hallucinations with Ditran were predominantly auditory, while those with LSD were mainly visual. Those with Ditran seemed to be more disturbing to the subject than those occurring in response to LSD. Subjects who developed psychotic reactions to both drugs were able to remember most events during their LSD experience, whereas the Ditran experience was mostly lost to recall. With Ditran there was a relative paucity of emotional expression, verbalization and physical action, and a tendency toward a stereotyped response, whereas with LSD the opposite was the case.

The stereotyped Ditran sequence observed usually included an initial brief period of relaxation followed by restlessness at the time the subject began to experience odd sensations, heaviness of the limbs, and perhaps myoclonic jerks. Then, about 15 to 20 minutes after the injection, slurred speech, inertia, mild to moderate clouding of the sensorium and perhaps a complaint about breathing would occur. The height of the response was evident within one hour after the injection. The following manifestations were usual by this time: 1) Unresponsiveness, both to questions by the examiner and environmental occurrences; this reached an extreme degree of total unresponsiveness in most subjects, but fluctuated in all. All showed the striking phenomenon of brief lucid intervals lasting

10 to 30 seconds and occurring every three to five minutes. During these intervals they were able to respond with fair coherence. Most of the test responses could be obtained only during the lucid intervals. This unresponsiveness with lacunae of lucidity lasted until the antidote was given. 2) Rambling, incoherent speech. 3) Impaired recent memory, attention and abstracting ability on testing, with remote memory frequently intact. 4) Disorientation, mainly as to time and place. 5) Changes in perception involving the form, distance, movement and, occasionally, color of objects. 6) Motor inertia or abulia. 7) Slow aimless movements of hands and mouth. These observations indicate that Ditran and LSD produce markedly different clinical effects. The antidotes produced quite rapid reversal of the clinical effects, but only to a partial degree in most cases.

The following summaries of the observations in two subjects illustrate some of the phenomena observed:

Subject No. 3: This was a male, age 31, with a diagnosis of sociopathic personality disturbance and sexual deviation. Ditran was given first. During the pre-Ditran examination, he was cooperative, but worried about the procedure. He complained of a headache, which he could not describe clearly. He spoke of fear of heights, recurring thoughts about fellatio, and suspicious ideas about one of his brothers. His sensorium was clear; intelligence was estimated at bright normal level. He performed the tests in a meticulous fashion. Twelve to 15 minutes following administration of Ditran, he described movements of the room, and complained of feeling "woozy," "pins and needles," and tired. After 30 minutes, he was unable to follow long sentences and was frequently unresponsive when questioned. At times he would smile for no apparent reason. Speech became slurred and mumbling. Thought content appeared random and disjointed. He was very distractible. He was unable to answer the questions for testing sensorium. Brief intervals of partial lucidity were present; some answers to questions, mainly from the Jarvik Questionnaire, were obtained during these intervals, usually after many repetitions. Aimless movements of the hands and eating motions were noted. He was unable to perform the drawing tests, although he made some crude attempts after repeated reminders. He would lose the pencil, seem unable to see it before him on the table, and have difficulty in picking it up and holding it. He spoke of a green frog on the table and said that the sphygmomanometer was about to fall off the table, but his emotional expression was unchanged and he made no moves in connection with these statements. After administration of THA, reversal of the above disturbances began in about 10 minutes. He became attentive, seemed happier, and again performed tests carefully. Except for slight, occasional slurring, speech cleared. The content and sequence of thought were judged to be as before the Ditran. Coordination improved markedly, although a tremor of the hands persisted. He was able to recall events during the Ditran experience, including hallucinations of people in the room with white faces and crippled legs and people shouting.

Before receiving LSD, the subject was much as before Ditran, except that he related more easily to the experimenter and seemed less anxious. Following LSD, he soon complained that his head and teeth were hurting, of difficulty in breathing, and being unable to see anything. His voice seemed to express helplessness. He reported color changes, flashes of color, and designs. Then he began to appear relaxed, and smiled much of the time, while simultaneously complaining of feeling fearful and cold, and occasionally groaning. At times he coiled up under a blanket and rocked himself. Occasionally speech was slurred and sentences incomplete. Digit repetition, arithmetic, absurdities, and proverbs test items were handled with no impairment from pre-drug performance. He reported "a large fantastic animal with hundreds of teeth keeping many people cornered in the street." He was able to do the drawings, but movements were large, quick, and careless. After sodium succinate, there was marked flushing of face, neck and limbs for about one hour. He still hallucinated the fantastic animal for a few minutes, but had a brief sleep and was unable to remember it upon waking. He spoke of things distracting him and stated, "I just don't have much feeling." Affect seemed flat and there was some slurred speech and distractibility.

Performance test scores were as follows: Bender-Gestalt—before Ditran, 50; during, no performance (225); after THA, 61; before LSD, 56; during LSD, 79; after sodium succinate, 64. Draw-a-Person—before Ditran, 25; during, no performance (0); after THA, 25; before LSD, 31; after LSD, 17; after sodium succinate, 19. The reactions to both drugs were classified as psychotic, that to LSD on the basis of hallucinations, that to Ditran because of hallucinations and "toxic-organic" symptoms. This subject was unusual in

that he remembered his Ditran experiences and forgot some of his LSD experience.

Subject No. 5: This was a 35-year-old woman, with a diagnosis of personality trait disturbance, passive-aggressive type. LSD was given first. Before LSD, the subject was cooperative, appeared somewhat depressed, and stated that she was thinking of problems involving her father and a recent dream. Her test performance was perfectionistic. Soon after LSD was given, she became emotionally labile, alternating between smiling and tearfulness, requesting reassurance, and expressing fear of dying. She reported that objects changed in shape and size. She stated that she was afraid to express her feelings because she had to "hold on to contact with reality." She alternately felt chilly and perspired. She then experienced enjoyable visual illusions, described as "a wonderland, just float away and enjoy myself." From later statements, it is probable that she was having sexual fantasies, during which she hid her face and seemed annoyed by interruptions. Speech, organization of thought, and sensorium appeared intact on examination. Tests were performed in a perfunctory manner. She expressed resentment at the conclusion of the experience when the antidote was given. During the sodium succinate injection she immediately became flushed and reported intense discomfort. The injection was not completed because she seemed near panic. She was friendly and cooperative during subsequent testing. No illusions or fantasies were elicited. She checked her drawings for accuracy, stated that she still had some visual disturbance, and apologized for her difficulties. She inquired if she could have the injection again.

Before Ditran, she was again cooperative and careful. About 20 minutes following Ditran, she was drowsy, almost motionless, and vomited after becoming nauseated. Thirty minutes after injection she denied any worries and appeared relaxed and comfortable. She stated that she had many thoughts, but could not report any. She was unable to complete sentences, but would sometimes pick up the previous trend of thought a little later. (The lucid intervals were closer together than in other subjects.) Thought content appeared disorganized and speech was slurred. She maintained orientation only for person. Memory was fragmentary. Performance on problem-solving, detecting absurdities, and proverb abstraction was grossly impaired, except during brief intervals of clearness. Drawing performance was poor, especially with designs involving dots, and she completed the drawings only after much encouragement. After THA, the subject was calm and relaxed in a few minutes. She stated, "I'm content," and reported no worries or fears. Speech was occasionally slurred, but thought sequence was coherent and rational. Memory and orientation were normal, but she had difficulty grasping the goal in reverse counting, and performance in absurdities and arithmetic was not as good as in the pre-drug state. Digit recall and proverb abstraction were not impaired.

Performance test scores were as follows: Bender-Gestalt—before LSD, 51; during, 81; after sodium succinate, 62; before Ditran, 60; during, 132; after THA, 93. Draw-a-Person—before LSD, 24; during 22; after sodium succinate 27; before Ditran, 21; during, 15; after THA, 18. The reaction to LSD was classified as nonpsychotic, only illusions and fantasies being elicited. The Ditran reaction was considered psychotic because of "toxic-organic" symptoms. No evidence was obtained of visual illusions or vivid fantasies with Ditran.

There was no obvious relationship between the clinical or test effects of the drugs and psychiatric diagnosis. Content of thought seemed more often related to known conflicts or problems with LSD than with Ditran, but this difference may simply reflect the greater disorganizing effect of the latter drug.

Some differences in the effects of the drugs were also noted with respect to certain physical findings. Whereas LSD did not produce a statistically significant elevation in blood pressure, the mean rises in both systolic (10.5 mm Hg) and diastolic (7.1 mm Hg) blood pressure following administration of Ditran were statistically significant ($p < .01$). THA produced a significant reversal of this blood pressure change. Neither drug elicited a significant elevation of pulse rate, but the pulse rate after THA was significantly lower than during Ditran, the mean decrease being 11.5 beats per minute ($.02 > p > .01$). The Babinski sign and apraxia were noted in six patients with Ditran and in none with LSD. Babinski persisted in two patients after THA and apraxia in one. Romberg signs or marked sway were observed in five patients with both drugs.

TEST FINDINGS

Test-retest reliability and practice effects: The pre-drug tests were used to

TABLE 1

Test-Retest Reliability and Practice Effect (Based on Pre-Drug Tests)

	Mean		Rho
	1st Test	2nd Test	
Bender-Gestalt	68.4	69.5	.93*
Draw-a-Person	30.4	32.4	.50
Jarvik Questionnaire	6.3	6.3	.81*

* $p < .01$.

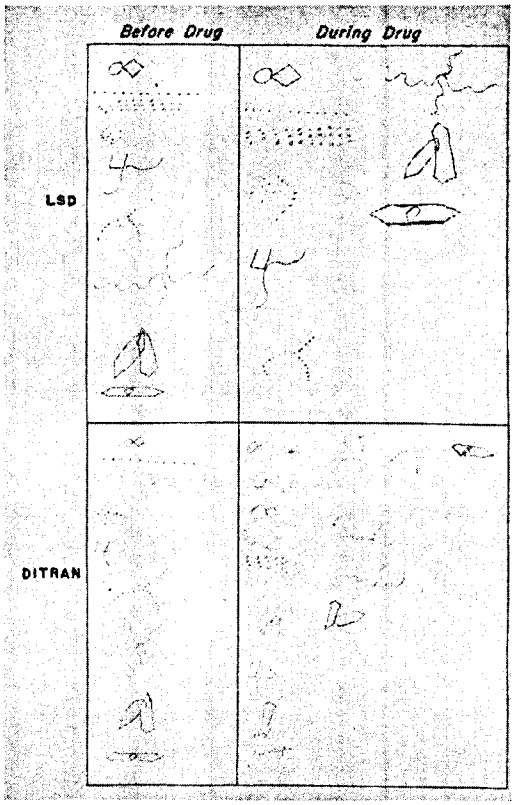

FIG. 1. Bender-Gestalt drawings of one subject before and after the administration of LSD and Ditran.

assess the reliability, or consistency, of test scores and practice effects. Statistical analysis for these purposes was based solely on the order in which pre-drug tests were given, *i.e.*, all first tests were compared with all second tests, without regard to which drug was given afterward. Rank-order correlation coefficients between first and second test scores and mean scores are given in Table 1 for the Bender-Gestalt and Draw-a-Person tests and Jarvik's Questionnaire (total number of positive answers). No significant practice effects were demonstrated. Only the Bender-Gestalt and Jarvik scores showed significant test-retest reliability. The Goodenough score was not significantly repeatable in this sample. It should be pointed out, however, that the range of scores was quite narrow, with most subjects scoring within a few points of one another. Furthermore, as the drug effects to be reported were relatively large and consistent, the low reliability of the Draw-a-Person test does not completely vitiate the significance of the changes which were observed.

Changes with drugs: Subjects experienced considerable difficulty in executing the drawing tests while under the influence of both drugs, but the disorganizing effect of Ditran was much more severe. Even with a great deal of urging, five of the eleven were unable to draw the Bender designs and six were unable to do figure drawings while under the influence of Ditran. By contrast all subjects were able to execute these tasks to some degree with LSD. Figures 1 and 2 reproduce the Bender-Gestalt designs and figure drawings of one subject who was able to draw with both drugs. The disorganization of performance is obvious, together with evidence of improvement in figure drawing after antidote administration. Table 2 gives the mean scores for the Bender-Gestalt, Draw-a-Person, and Jarvik tests under various conditions. As subjects unable to perform with Ditran could reasonably be considered to display a maximum degree of impairment with this drug, their tests were assigned arbitrary scores of 225 for the Bender-Gestalt and zero for the Draw-a-Person. These were somewhat worse than the poorest scores achieved by subjects able to draw. The mean values for the drawing tests are shown in Figure 3.

The mean changes in test scores produced by both LSD and Ditran were all statistically significant ($p < .01$). In all 11 cases, each drug produced impairment on both drawing tests. Also, without exception, performance was poorer with Ditran than with LSD. The Jarvik total score was increased in all cases except for one Ditran subject, who showed no change. The antidotes produced a partial reversal of the psychotomimetic test changes. THA, following Ditran, brought about a significant improvement in drawing performance and reduction of symptoms elicited by the Jarvik ($p < .01$). Sodium succinate produced similar reversals after LSD, but only the Jarvik score change attained statistical significance ($p < .05$). Although the Bender-Gestalt score was improved in all six cases to whom sodium succinate was given and the Goodenough score was improved in five, the mean changes were significant only at the .10 level.

Comparing the effects of Ditran and LSD, the Jarvik Questionnaire results differed from those obtained with the drawing tests. The latter showed a much greater disorganizing effect of Ditran, whereas the effect of both drugs on the total number of questionnaire responses was about equal. To determine whether there was a difference between drugs in the kind of responses elicited, a separate analysis was carried out for the Jarvik questions dealing with physical, perceptual and cognitive symptoms. The mean changes in scores with each psychotomimetic are given in Table 3. Whereas the the increases in physical and perceptual

TABLE 2

Mean Test Scores Before and after LSD and Ditran, and after Antidotes

	LSD			Ditran		
	Pre	During	After*	Pre	During	After
Bender-Gestalt	69.9	112.3	77.2	68.1	193.7†	100.8
Draw-a-Person	31.6	19.9	25.0	31.3	6.6‡	24.0
Jarvik (Total)	6.3	21.1	9.5	6.3	17.5	9.3

* Six cases only.

† Includes 5 assigned scores of 225 for subjects unable to perform.

‡ Includes 6 assigned scores of zero for subjects unable to perform.

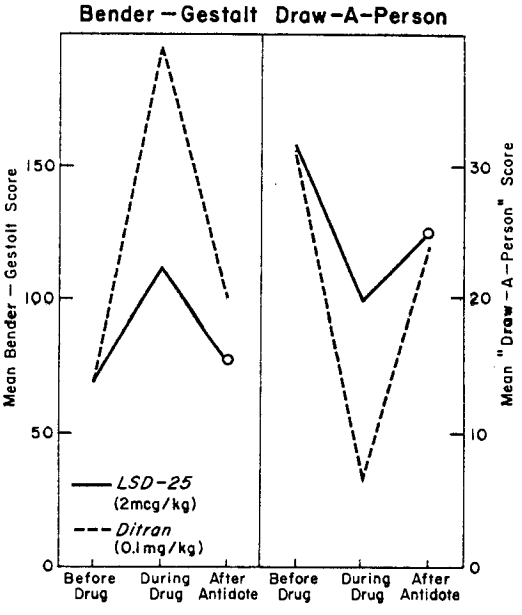

FIG. 3. Mean Bender-Gestalt and Draw-a-Person test scores before and during LSD and Ditran and after antidote administration. Only six subjects received sodium succinate after LSD (open circle).

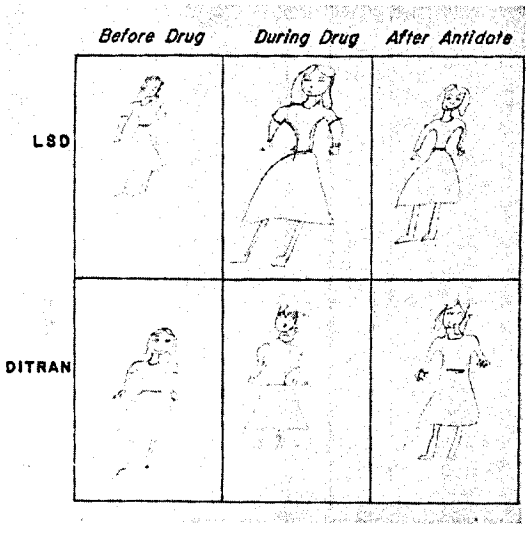

FIG. 2. Figure drawings for same subject as Figure 1.

TABLE 3

Mean Score Changes in Subsections of Jarvik Questionnaire

Question Type	LSD	Ditran
Physical	4.4	5.1
Perceptual	9.3	6.3
Cognitive	1.6	0.3

TABLE 4

Rank-Order Correlations (Rho) between Test Score Changes with LSD and Ditran

	Rho
Bender-Gestalt	.20
Draw-a-Person	.54
Jarvik—Physical	.06
Perceptual	.67*
Cognitive	−.02
Total	.44

* $.05 > p > .02$.

scores were significant for both drugs ($p < .01$), the cognitive changes were not significant for either. The mean perceptual score changes were significantly greater for LSD than for Ditran ($p < .05$). This finding agrees to some extent with the clinical observations concerning illusions described above.

To evaluate the question of consistency in individual susceptibility to the two psychotomimetics, correlations between changes in test scores produced by each drug were determined. The coefficients are shown in Table 4. The only one statistically significant was that for the perceptual symptoms on the Jarvik Questionnaire. This suggests the presence of some tendency for individuals to maintain their order of sensitivity to perceptual changes with both LSD and Ditran, even though LSD produced more responses in this sphere. The correlation data for the drawing tests are open to question on the grounds that about half of the subjects had to be assigned arbitrary scores for the Ditran effect. However, rank-order correlations calculated only for those who could draw were approximately the same as those in Table 4. Also, there was no significant difference between the mean change scores with LSD of those subjects who could and could not draw with Ditran. These findings support the conclusion that there was no significant individual consistency in susceptibility to impairment of drawing performance by the two drugs. Additional indirect evidence in support of this conclusion is the fact that, with LSD, the scores before and after drug administration were significantly intercorrelated, with coefficients of .83 and .65 for Bender and Goodenough scores, respectively, whereas half of the subjects could not draw at all with Ditran, and their pre-drug scores ranged from low to high. This means that subjects tended to retain their relative performance position while under the influence of LSD, whereas the performance order was eliminated by Ditran.

DISCUSSION

Our findings indicate that, in the doses given, there are marked differences in the effects of Ditran and LSD. Present observations on the clinical effects of Ditran agree well with those of Meduna and Abood (13), Bercel (3), and Hollister *et al.* (8); all subjects could be considered to develop a "toxic-organic" reaction or delirium. Similar changes in speech, responsiveness, memory and orientation were observed in only a few subjects with LSD and to a much lesser degree. In contrast to the stereotyped sequence of the Ditran response, there was considerable variety of behavior with LSD. Although both drugs elicited perceptual changes, these were similar only during the early phase of drug reaction. During the later phases, the illusions with Ditran were less vivid than with LSD, and hallucinations were usually auditory with Ditran and visual with LSD. The responses to Jarvik's Questionnaire suggested greater perceptual change with LSD, but it should be borne in mind that this questionnaire was designed to reveal LSD effects. Certain physiological changes, as reflected in blood pressure,

Babinski sign, and apraxia occurred with Ditran, but not with LSD. Ditran also produced greater disorganization in performance on the drawing tests, and altered the between-subject order of performance ability whereas LSD did not.

Virtually all findings with Ditran were thus consistent with interpretation of the reaction as "toxic-organic" in type. The LSD reaction could not so readily be classified, as more of the symptoms resembled those found in "functional" psychotic states. As observed by Pauk and Shagass (15), the drawing test changes with LSD often resembled those reported in brain syndromes, but were not closely paralleled by the clinical findings.

One may question whether the differences between drugs would be diminished by use of different doses. Would a lower dose of Ditran and a higher dose of LSD have produced more nearly similar effects? This possibility cannot be ruled out. It may be pointed out, however, that the present Ditran dosage, 0.1 mg/kg, was less than that used by most other investigators. Gershon and Olariu (6), for example, gave 0.2 mg/kg. Also, the incidence of psychotic reactions with the present dose of LSD was the same as found with higher doses by Pauk and Shagass, and the mean changes in drawing test scores were about the same. This suggests that the LSD reaction pattern would not have been much different with higher doses. The effects of smaller doses of Ditran remain to be explored.

The antidotal effects of THA for Ditran and of sodium succinate for LSD were supported by present clinical and test findings. Although the Ditran changes were not fully reversed by THA, it should be noted that the 30 mg dose used here was only half that employed by Gershon and Olariu (6). A larger dose of THA might have been more effective. Sodium succinate reversal of LSD changes was also partial, but one wonders to what extent the marked discomfort produced by this agent could have been responsible for some residual effects.

The idea of a factor which may govern individual susceptibility to all psychotomimetic agents was not supported by present findings. This conclusion is indicated by the relative variability of LSD response and stereotypy of Ditran effect in the same population, and by the absence of correlation between changes in the performance test scores. The fact that half of the subjects unable to execute the drawing tests with Ditran developed a psychotic reaction with LSD and the other half did not, also suggests a lack of concordance in susceptibility. On the other hand, present data cannot be taken to settle the issue of a susceptibility factor. It is possible that other tests, lower drug dosage, and perhaps comparison of different psychotomimetics might reveal evidence of one. Under the conditions of the present study, "drug-specific" far outweighed any "person-specific" factors.

SUMMARY

A comparative study of the effects of two psychotomimetic drugs, LSD and Ditran, was carried out in 11 nonpsychotic psychiatric patients. Continuous clinical observations were made following each drug injection, and Jarvik's Questionnaire, the Bender-Gestalt and Draw-a-Person tests were serially administered. The antidotal effects of sodium succinate for LSD and of tetrahydroaminacrin (THA) for Ditran were also evaluated.

Results indicated marked differences between the effects of LSD and Ditran. The latter produced, in all subjects, a relatively stereotyped series of behavioral changes closely resembling a "toxic-organic" reaction or delirium, and accompanied by blood pressure elevation and frequent Babinski sign and apraxia. Only six of 11 subjects developed a reaction to LSD meeting our criteria of psychosis and the behavioral responses were much more variable than with Ditran. Performance on drawing tests was

impaired by both drugs, but impairment was much greater with Ditran. The only difference between drugs revealed by the Jarvik Questionnaire was a greater change with LSD in the perceptual sphere. Sodium succinate and THA, respectively, reversed the clinical and test changes produced by LSD and Ditran, but not completely. It was concluded that present data did not support the concept of a general factor governing individual susceptibility to psychotomimetic agents.

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