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The Response of Normal Men to Lysergic Acid Derivatives (Di-And Mono-Ethyl Amides)*

Correlation of Personality and Drug Reactions

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Considerable interest has been shown recently in the production of an "experimental psychosis"[1] or "schizophrenia-like symptoms"[2] by drugs. Three agents have figured prominently in such reports: mescaline, lysergic acid diethylamide, and lysergic acid ethylamide. The first is derived from the peyote cactus while the latter two are members of the ergot group. The hope underlying this work has been to increase understanding of the psychologic and physiologic factors involved in psychotic states by reproducing such states experimentally in a controlled situation.

This is not a new approach. In 1904, Peters[3] reported on the cataleptic action of bulbocapnine in animals. In 1930 de Jong and Baruk[4] confirmed this observation and studied this drug and related chemicals with reference to their catatonic effect in man. However, progress lagged until the discovery of new chemicals and compounds, notably the three mentioned previously. These have stimulated new work which Rinkel, DeShon, Hyde, and Solomon[5] have hailed as opening a new field of experimental psychiatry.

Experimental work has been interpreted by some to support those views that assume endogenous chemical substances to be the cause of schizophrenia. Thus Rinkel and his associates[2] state, "It may be possible to assume that fundamentally the mechanism of origin of natural and experimental psychotic phenomena is a similar one." Much of the work in this area has been with psychotics or severely disturbed patients. The general conclusion drawn has been that in psychotics the drugs elicit the latent or accentuate the existing schizophrenic symptomatology. Work with normal subjects has been less frequently reported and the predrug individual personality structure in such persons has not been related to the drug effect. This is our principal interest. The present report describes the results following administration of lysergic acid diethylamide to 10 young healthy male subjects and lysergic acid ethylamide to 9 similar volunteers, and the relationship of these results to the personality of the subjects.

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PREVIOUS REPORTS

LYSERGIC ACID DIETHYLAMIDE

Lysergic acid diethylamide and lysergic acid ethylamide are both semisynthetic ergot alkaloid derivatives. Lysergic acid ethylamide[5] differs from lysergic acid diethylamide in having only a single ethyl group, whereas lysergic acid diethylamide has two such groups. The capacity of lysergic acid diethylamide to produce marked psychologic reactions was first observed by Hofmann, who inadvertently inhaled a minute amount while working with the drug and became acutely intoxicated, with great fantasy production. Hofmann's experience led to Stoll's[6, 7] investigations of lysergic acid diethylamide. He reported that the drug produced the most profound psychologic disturbances: hallucinations, compulsive thought and speech, and alteration of consciousness. He regarded this as a psychotic condition and suggested the term "Phantasticum" for the drug. Becker[8] suggested that "Psychoticum" would be more appropriate.

In subsequent investigations[2, 6–12] systemic effects have been reported as similar in both normal and psychopathic subjects; however, a wide range of psychologic effects are described. Unfortunately, it has not always been clear whether descriptions refer to the normal as well as the psychopathic subjects. In general, the following psychologic features have been mentioned. Consciousness and general orientation are reported as maintained, although sometimes clouded. A feeling of "intoxication" is described. Judgment, memory, and other intellectual processes appear to be undiminished. Insight as to the drug origin of the effects is usually maintained and so is "contact with reality." Ideas are variously reported as stimulated with some confusion, or slowed down and inhibited. Along with this is a general reduction in the power of attention and loss of efficiency in concentration. With regard to mood effects, some authors report striking euphoria with manic behavior. Involuntary laughter has commonly been observed. Euphoria is often associated with physical activity, but passive and apathetic euphoric moods are also reported. Depressive reactions are frequently reported. The signs of depression may be associated with tears, resentment, and aggressiveness, or a passive withdrawn or indifferent behavior.

A frequently reported effect is the "wave-like" or periodic and recurrent nature of most of the reactions. Alternate phases of euphoria and depression are also recorded. Early reports stressed the euphoric reaction with an acceleration of mental activity, but later work has revealed more frequent depression and associated "slowing up." Paranoid trends have been described.

Perceptual changes have been emphasized by most workers and "hallucinations" are generally reported. These, however, might better be described as elementary perceptual distortions (perspective changed, shadows and contours fuzzy, with paling of colors) rather than as true hallucinations. In our subjects there was never any loss of contact with the real situation. Upon closing the eyes many subjects have seen flashes of light or lines and sometimes geometric figures, as after mescaline,[1] or have seen figures and objects. Hyperacousia is reported and false interpretation of noises has been found. A few cases of tactile "hallucination," e.g., a sensation of being wet, are described.

The term "depersonalization" is also used by previous authors to denote an assortment of general bodily feelings, for example, heaviness of limbs, limbs seeming longer, numbness, etc. Several writers state that the depersonalization amounts to a true split personality. This is described as of a clearly schizophrenic nature, with subjects feeling that their real self had changed and that they were cut off from the rest of the world.[1, 6-8]

Two workers have carried out Rorschach testing on subjects during lysergic acid diethylamide intoxication. Stoll,[13] reporting on 11 normal adult cases, concludes that the Rorschach changes are typically those of organic deterioration, although some are suggestive of schizophrenia. DeShon, Rinkel, and Solomon,[10] studying 5 normal subjects, concluded that the changes were principally of the schizophrenic or paranoid type.

In general, then, investigators to date have considered the symptoms of lysergic acid diethylamide intoxication as the expression of an acute exogenic psychosis, consisting of a mixture of hypomania in the area of "intention" functions and schizophrenia in the areas of "affect."

Since in psychotics, symptoms tend to be exaggerated, it has been seriously suggested that lysergic acid diethylamide be used as a diagnostic personality test, revealing the cyclothymic as a manic-depressive and the schizoid as a true schizophrene.[7-9] Indeed, it has been recommended to the psychiatrist as an aid in self-analysis, providing him with an experiential sample of his patients' symptoms.[7, 8] There has apparently been some reluctance on the part of therapists so far to avail themselves of this aid.

LYSERGIC ACID ETHYLAMIDE

In 1953, Solms[5] reported on a "new antipsychotic drug with strong sedative effect," lysergic acid ethylamide. In his study of 8 normal men, he reported a triphasic reaction. The first phase (of 15 minutes' duration) consisted of "benign neuro-vegetative irritation" and mild discomfort such as salivation, tears, sweating, ataxia, hyperreflexia, and paresthesias. There was occasional nausea, heavy breathing, and sensation of vibration and tension in the muscles. The second phase (of one to two and a half hours' duration) was one of "psychosis," with a sudden onset of personality changes and simultaneous disappearance of discomfort. The psychopathologic symptoms were primarily those of a schizophrenic-like asthenia, indifference, and intensive phenomena of depersonalization without sleep. Solm's report is, we believe, the only one to date on lysergic acid ethylamide, and contrasts lysergic acid ethylamide with lysergic acid diethylamide. He reports three main differences, but emphasizes that "none of these differences involve questions of principle:"

1. Lysergic acid ethylamide must be given in larger doses (10 times or more) than lysergic acid diethylamide to produce effects.

2. Optic distortions and hallucinations are more frequently seen after lysergic acid diethylamide.

3. Apathy and decreased motivation are more frequent after lysergic acid ethylamide, lack of inhibition and excessive drive being more characteristic of lysergic acid diethylamide.

Solms considers the profound disturbances of the ego to be the basic effect of both drugs

with depersonalization the chief symptom. He states: "It seems to us that such a falling apart of the body-soul unity shows up more frequently and more intensely under lysergic acid ethylamide than under lysergic acid diethylamide."[5]

METHODS AND RESULTS OF PRESENT STUDY

This report deals with the results of administration of lysergic acid diethylamide to 10 healthy male subjects and of lysergic acid ethylamide to 9 similar subjects. Interviews and Rorschach examination of all 10 lysergic acid diethylamide volunteers were obtained both before and during the drug-induced state, and during the nondrug state for 7 of the lysergic acid ethylamide subjects.

I. *Lysergic Acid Diethylamide*

A. *Dose and Route:*

In all instances, lysergic acid diethylamide was given by mouth, in either the fasting state or after a light breakfast. When food was ingested, the time between breakfast and taking of the drug was of sufficient length to make it appear unlikely that absorption was materially affected by the meal. The oral administration of drugs is notoriously less reliable and predictable than the use of parenteral routes, but was adhered to in view of the absence of data on the safety of lysergic acid diethylamide when injected into man. Total doses employed by other authors have varied from 20 gammas[12] to 500 gammas.[14] Most have received 20 to 90 gammas. In our studies, total doses varied from 39 to 86 gammas (most patients receiving one gamma per kilogram of body weight). Thus, both in respect to dose and route, our study is comparable to those previously reported.

B. *"Physical" Effects:*

Changes in vital signs were of slight moment when present and difficult to separate from the changes observed in accommodation with time to a stressful situation, or to increase of ease and rapport with the laboratory personnel, anxiety, or other responses to the effects experienced. With the doses and route employed, cardiorespiratory changes were usually of no consequence in our healthy adult male group. An exception to this statement was observed. In one subject, a tense student with many conflicts, an interview having a mildly probing nature resulted in considerable anxiety during the period following drug administration. Shortly after the anxious state appeared, the subject had a vasomotor disturbance with pallor, cold clammy skin, nonpalpable pulse, slight convulsive movements of the face, and stiffening of the body. (In other studies we have observed a similar state upon injecting a placebo.) The whole episode was over within 30 seconds or so, and was not followed by confusion. The patient had experienced fainting spells before, but had no history of personal or familial epilepsy. Our interpretation of the episode was a syncopal attack (possibly secondary to emotional stress) followed by cerebral ischemia and its manifestations. A subsequent electro-encephalogram on this subject was interpreted as normal.

Giddiness was experienced by 6 subjects, especially on standing. Five subjects had gross tremor of the outstretched hand, with sometimes a subjective feeling of tremulousness. No gross incoordination, ataxia or positive Romberg's sign was evident, although 5 subjects

complained of unsteadiness and decreased coordination. Paresthesias (if one includes all descriptions of numbness, tingling, heaviness, warmth, cold in various parts of the trunk and limbs) were seen in all but 2 of our patients. A curious but very frequent experience was the feeling that these paresthesias would come and go in "waves." Two subjects felt hot or cold or perspired.

Headache or neckache occurred in half of the subjects. Three of the group had vague abdominal or substernal "feelings." One subject had marked and prolonged retching and vomiting following waves of nausea. One subject had an increased desire for food, but said it had no taste for him. Only the subject described previously (under blood pressure changes) became pale. Two subjects complained of a dry mouth. Two subjects felt sleepy, but none actually dozed off.

C. *Mental Effects:*

1. Mood:

Four of our subjects experienced some inner tension or anxiety. Half of the subjects had a mild or marked desire to laugh or were amused without cause, 2 of them actually laughing out loud and smiling for long periods of time, despite an apparent lack of feeling of inner happiness or joy. These 2 subjects described their facial muscles as having an independent, essentially uncontrollable action of their own. Only 2 of the patients had really pleasant, euphoric reactions. One became expansive and experienced a strong sense of well-being, and another had pleasant bodily sensations with some erotic content. Another subject had marked erotic and pleasant illusions, but mixed with these were anxiety, apprehension, and paranoid trends. No one became really depressed.

2. Thought and Speech Processes:

In our experience there has not been an increase in thought or speech processes (expressed or unexpressed), but rather a slowing down of speech and expression, confusion, difficulty in concentration, and in remembering what has been read or written. One patient observed "increased distractibility." Several have phrased it somewhat differently as "difficulty in paying attention." Eight of the 10 subjects showed this type of response. A possible example of the opposite type of response was one subject who felt that he was speaking a lot more than before, although this was not obvious to the investigators.

3. Perception:

The subjects in our study have not shown any true hallucinations. Three of the subjects had vivid visual illusions, one with markedly erotic and another with somewhat erotic content, but no subject at any time felt that these illusions were real. No other hallucinatory experiences were reported, but several subjects complained that their depth perception seemed to be off, that objects seemed to be indistinct or smaller in size, or that they had persistent after-images. In a few of these latter subjects, a possible explanation for visual disturbances was found in a marked mydriasis which responded sluggishly to light and accommodation. These changes have been reported on occasion by other observers.

4. Miscellaneous:

Some observers have found a tendency for subjects to experience a sensation that they were "outside of themselves." Some of our subjects also stated that at times they seemed

to be "observing someone else doing what they were doing." No real depersonalization, however, was found in any of our subjects.

II. *Lysergic Acid Ethylamide*

A. *Dose and Route:*

Of our group of 9 subjects, 3 were given a total dose of 0.25 mg. and 6 were given 0.5 mg. of lysergic acid ethylamide, all doses being administered subcutaneously. In the only other published report on this drug[5] 8 subjects were given from 0.5 to 0.75 mg.

B. *"Physical" Effects:*

There were no alarming changes in vital signs, although one subject did show a rise in blood pressure from 125/55 to 165/85, in pulse rate from 82 to 130, and in respiratory rate from 18 to 25. Three of the subjects showed no changes in vital signs and one had a slight gradual decrease in blood pressure and pulse over the several hours required for testing (possibly due to inactivity or decrease in predrug anxiety). Most of the subjects (5) have had a transient hypertension, tachycardia, and tachypnea, suggestive of epinephrine release.

Of the "physical" effects, the outstanding ones were nausea (7 subjects, one of whom also vomited), paresthesias (7), dizziness (6), feelings of warmth (3) or cold (1), and salivation (2). In addition, one subject complained of palpitation, one had a transient paroxysm of coughing, and one complained of a sore throat.

C. *Mental Effects:*

The mental change occurring most frequently was a "dulling of the senses," present in 7 of the 9 cases. This was sometimes described as "grogginess," or "a confused feeling." The subjects also complained of difficulty in reading or concentrating. Five of the subjects stated they were sleepy, 4 that they felt "lazy," 5 were "shaky," "apprehensive" or "restless," and 3 had a strange combination of simultaneous energy and lassitude. Two persons described their muscles as relaxed and "rubbery." Two others said they felt "light and buoyant."

The most interesting change observed (in 4 subjects) was a period of hostility with paranoid tendencies.

Three of the subjects considered their reactions pleasant, 3 unpleasant. One of the latter had a panic reaction with intense agitation and overwhelming fear. His reaction was so intense as to require the administration of an intravenous barbiturate. One patient said he had "an overwhelming desire to talk."

Two types of reactions were reminiscent of some responses seen after lysergic acid diethylamide administration: (1) a tendency to feel amused or to laugh out loud (5 subjects), and (2) the description of some symptoms as recurring in "waves." The only finding at all suggestive of the visual illusions so commonly described after lysergic acid diethylamide (and seen in a few of our own subjects who received the latter drug) was observed in one subject who described objects as "looking pallid" and lacking their normal coloration.

RORSCHACH DATA

I. *Lysergic Acid Diethylamide*

All lysergic acid diethylamide subjects were given a second Rorschach examination while

under the effects of drugs. The first Rorschach* examination was given before the drug was administered, as previously described. These tests were given usually several hours after the drug ingestion when the observers believed the symptomatology was either at its peak or just receding. Seven of the 10 subjects showed distinctive changes in the determinants of their responses. (In an extensive study of the so-called ego-depressant drugs, this is the first time we have found a fairly consistent modification of the Rorschach response by the drug.) In 6 of these 7 cases the changes were in the same direction and of similar meaning. In general these changes took the form of an expansive release phenomenon in which the post-drug Rorschach was an exaggerated caricature of the predrug one, whereby previous weakness of ego functions was particularly magnified. Intellectual processes tended to regress to an immature level. Thus animal movement responses (FM) became dominant over human movement responses (M). This was particularly evident where the predrug balance was stable or M not especially dominant. Since M dominance is a normal concomitant of mature development, this reversal indicates regressive and immature thought processes, as wel as a weakening of intellectual control over affective and emotional impulsivity. In adults too, the degree of FM dominance correlates with the degree to which productive potential is wasted. The same regressive phenomenon is reflected in the shift in color responses from FC to CF and in a few cases, to C. In adults FC responses should be dominant. They reflect the development in behavior of increased restraint in the regulation of the forms of self-expression, and the modulation and restriction of the behavioral and emotional impulsivity and unpredictability characteristic of younger age groups. These post-drug changes seriously undermined the characteristic mechanisms developed by each personality for the control of behavior and for defense against anxiety. Under these conditions perceptual processes were correspondingly altered with an accentuation of emotional states at the expense of external reality factors. The fact that only 3 subjects of these 7 experienced sensory illusions seems surprising.

The M:ΣC ratio, reflecting the balance of affective and regulatory spheres in the personality (optimally within 2:1 to 1:2 range), was seriously unbalanced under the drug, the median ratio for the 7 cases being 1:3.5 before and 0:7.5 following the drug. This severe threat to self-control was reflected in the experience of tenseness, anxiety, and "jitteriness," as well as the stated fear of losing control.

As indicated above, the degree to which the Rorschach was changed was positively cor-

* Rorschach scoring used here is based primarily on Klopfer and Kelley.[15] Scoring is in terms of determinants of the response: form (F), movement, human and animal (M and FM), color (C), more or less integrated with form (FC, CF), shading (c) and achromatic color (C′), etc. Interpretation of the determinants is derived from empiric demonstration and from consideration of genetic development. For example, response to color in the cards is empirically related to the initiation of affective experience, and genetically, color responses develop from pure C responses at about 3 years of age to a gradual occurrence and dominance of CF at approximately 6 or 7, followed by a gradual increase of FC responses which normally become dominant over C and CF in the postadolescent period. Interpretation of an individual record depends, however, not only on this rationale, but also upon the context of other determinants in a record. Principles involved have been extensively discussed by Phillips and Smith.[16]

related with the relative weaknesses of personality development already present. Significantly too, the total amount of reaction to the drug (in terms of objective evidence and subjective description) was also highly correlated with a "maladjustment" ranking by the psychologist based on an interview and the predrug Rorschach test. The correlation between these maladjustment rankings and the drug reactivity rankings by the pharmacologist was .93. Rankings by the pharmacologist and by the psychologist were performed independently of course.

Two cases illustrate particularly well the psychosomatic relationships involved. Subject X, already mentioned, who had the syncopal attack, was a chronically driven and tense individual given to compulsive hyperactivity, intellectually, physically, and socially. The reasons for his neurotic manifestations and distinctive defensive mechanisms were not adequately revealed during the predrug interview and testing, but this predrug probing did not result in more than a slight increase in tension and forced jocularity. The predrug Rorschach record of this subject contained only one color response, a pure C. Empirically, pure C responses occur most infrequently in normals, and then only in "impulsive" and "explosive" normals. In the absence of other more mature color responses, pure C responses suggest pathology, possibly of an "organic" nature. After lysergic acid diethylamide, this subject gave four pure color responses of violent fire or blood content. A negative Phillips Fx score,[17] which has been demonstrated to be associated with assaultiveness, was present in the predrug Rorschach (—1.5) and increased postdrug (—5.5). His M:ΣC ratio went from 1:1.5 to 1:6. Seen in these terms, the seizure experienced by this subject is strongly suggestive of an "emergency discharge" of unbearable inner tension, much as the epileptic syndrome probably functions as an emergency outlet in certain constitutionally predisposed individuals.[18]

Subject Y is notable for his vivid and erotic visual "hallucinations:"

12:34 p.m. (Two and a half hours after 60 gammas of lysergic acid diethylamide). Sees dots in round circles (eyes closed). "My face and muscles are twitching—I seem to be talking an awful lot. I don't want to open my eyes, but I don't know why." Sees streaks of wavering gray on ceiling (eyes open). "Oh, it's just the shadow of the blind—it took me a while to figure that out."

12:45 (Eyes closed.) "I see red and green lights like Christmas tree lights against a black background. Opening your eyes brings you back to reality."

12:50 "My eyes are closing as tightly as they can. It feels like cramps. I don't want to open my eyes because I can think freely and it's sort of a mental pleasure—like driving a car at high speed—there's a little Frenchman driving and I'm the passenger."

1:30 Patient given tachistoscopic word perception test. His responses are confused by erotic fantasies visualized when looking into the machine—man and woman kissing, in erotic play, scantily clothed people.

2:30–3:00 Continued sexual images. States fear of having "come off in pants" during images at tachistoscope. Finally feels shorts to see if true (not). "Definite sensation of wet pants."

3:00 Can still see erotic movements, but "I'm all played out." Face feels heavy "as after an enormous drunk. I'm apprehensive after you (psychologist) leave the room. I'm afraid you won't come back. I tremble and sweat. I don't know whether you are testing me or the drug. Maybe it's for my father, or the army or for (college)." Needs considerable reassurance.

Seen in terms of the interview and predrug Rorschach, this subject was immature and

chronically anxious, dominated by sexual fantasies and impulses of a strong homosexual and anal nature. The act of volunteering for the experiment itself had strong "seductive" overtones for him as a possible erotic experience in a guilt free atmosphere. Under the drug these dynamics blossomed out. Rorschach responses demonstrated the collapse of initially weak control functions and defenses.

The content changes in the Rorschach give some example of this:

Predrug	Postdrug
Card IV	
1. Upper part looks like the top view of genitals.	1. X-ray of top of ram's head.
2. Back of a chicken.	2. These wrinkles suggest the end of a penis, these are testicles, they're pretty weird—warped.
	3. Multi-photo of a woman twisting around, arms out at angles.
	4. Faces of women—one looking down askance at other.
	5. Legs—looking up at them.
Card VI	
1. Back of a man.	1. Underneath view of a man with erection—looking up—see the anus, penis—rest of card is flesh.
	2. A black figure in the background—a statue of a man—young, hands at side—it's a little boy of 14 with a pack on his back.
	3. Foot—on its toes.
Card VII.	
1. Back of woman.	1. Don't know whether it's a male or female—looks like the anus.

Superficially, this case is an exception to our Rorschach scoring trends since on the predrug testing he gave three immature color responses and in the posttesting no color responses at all. However, since genetically the period in which no color responses are given precedes the stage at which they are elicited, in this sense the absence of color perhaps represents an even further regression to a lower genetic level than does the shift from mature to immature color responses.

Both of these cases illustrate what seems to be a primary psychologic effect of the drug—the exacerbation of existing symptomatology through a weakening of control functions and defense systems.

II. *Lysergic Acid Ethylamide*

Predrug Rorschach testing and interview were given to 7 of the 9 lysergic acid ethylamide subjects. Again independent ranking by the psychologist and pharmacologist revealed a high correlation (.80) between "maladjustment" and degree of drug "reactivity." The 3 best adjusted individuals (ranks 1, 2, 3) had no, or extremely minor, effects, and this group of subjects did not scatter so widely along the adjustment-maladjustment continuum as did the lysergic acid diethylamide subjects.

The range of reactions and particularly their intermixture in this small sample precludes the analysis of drug reaction and personality structure. However, the 4 subjects who had paranoid or hostile reactions to lysergic acid ethylamide and the single subject responding in like manner to lysergic acid diethylamide deserve special comment, since the reaction has not been seen (when consciousness was unimpaired) in this laboratory during the study of other drugs. An analysis of the predrug Rorschachs (on 4 of the 5) indicates that while none of them could be called "paranoid" (except by analytic implication from homosexual trends in 2 of them) the incidence of "looking," "watching," and "eyes" responses in essentially guarded records is suggestive of suspicious attitudes in interpersonal relations. While this implies psychologic predisposition it is noted that one of these subjects had participated in other drug experiments involving five drugs and this reaction had never been noted. He was, however, atypical in his reactions to several of these drugs, where uniformity of reaction was more common among subjects than in the present experiments.

DISCUSSION

In regard to the comparison of lysergic acid diethylamide and lysergic acid ethylamide, our experiences only partly confirm those of Solms.[5] The doses of lysergic acid ethylamide utilized by us were many times greater than those of lysergic acid diethylamide, but no striking difference in severity of symptoms was seen. This would tend to confirm Solms' statement about differences in potency. Our data on perceptual distortions also suggests that this author's second statement about the rarity of optic "hallucinations" after lysergic acid ethylamide (as compared with lysergic acid diethylamide) is similarly correct. His third differentiation (relative to differential mental effects), however, cannot find confirmation in our data. Both lysergic acid ethylamide and lysergic acid diethylamide seem to produce a general slowing down of mental processes in our subjects. Both drugs show remarkable power in producing definite psychologic changes. While in our experience these changes are not unique and other drugs have, in this laboratory, produced symptoms of even greater degree, the incredibly small traces of lysergic acid diethylamide that are sufficient to effect change is of considerable significance. Those investigators who choose to view these drug reactions as "psychotic" or "schizophrenic" see in this fact considerable support for the conception of schizophrenia as an endotoxicosis. Our own experience with this drug, while limited, does not give much support to such a view since with one exception (suspiciousness) the symptoms observed under this drug are not unlike those produced by other agents and do not, in our estimation, constitute psychotic processes to any greater extent than those produced by other drugs. In this regard it seems important to emphasize the maintenance of voluntary control and, more particularly, of insight and the capacity for reality testing throughout the drug reaction by our subjects.

The relationship of the predrug personality structure and the type of drug reaction was not as apparent with these drugs as with some other we have studied,[19] but the correlation of the amount of induced change and the degree of pre-existing maladjustment implies the presence of significant relationship. This finding suggests McFarland's[20] work on anoxia where he found a high correlation in neurotics between symptom formation, including

physical collapse, and low levels of anoxia (induced by simulated high altitudes) where the normal individual was unaffected.

It is important to keep in mind when evaluating drug reactions that the primary drug changes can constitute a stressful situation for particular individuals and they may react with vigorous restitutive activity.* The complete drug reaction may then be best explained in terms of the individual's defense system or his characteristic reaction to stress or threat in general. The paranoid reactions are a case in point. Thus it might be expected that the poorly adjusted individual would react to drugs with greater diversity and more intensity of behavior than other individuals.

It is easy to appreciate the role of psychologic factors in the "secondary" drug reactions which sometimes supersede the initial, expected one. These reactions are most easily understood as the result of the integrative functions of the personality acting to adjust behavior to an acceptable compromise between internal processes and reality demands or, stated another way, constitute restitutive efforts on the part of a threatened personality organization to preserve its integrity or re-establish its equilibrium. Altering the internal components of this balance may create fear or panic and great efforts may be made to integrate the change in an emotionally acceptable manner. This may be the best explanation of religious revelations following ritual drugs and philosophic formulations during the use of mescaline.

The above situation seems analogous to psychologic defense mechanisms developed as a result of threatening disturbances of intrapsychic mechanisms or interpersonal relationships. The defense mechanism of denial is an example in point. It is an interesting, but unexplained, observation in our drug experiments that denial appears to be most frequently employed by subjects characterized by a psychopathic personality structure. Another observation of this laboratory is that panic or near-panic as a reaction to drugs seems characteristic of personalities struggling with very strong sexual problems, primarily those of a homosexual nature.

The use of drugs to produce a "psychosis in miniature"[1] and to produce secondary defense reactions in order to study experimentally the relationship of defense pattern and its determinants offers interesting possibilities. An extreme example of drug effect on the development and choice of defense mechanism was the reaction of a young college student (following lysergic acid diethylamide) whose integrative efforts during the drug sessions constituted "the most important experience of my life." The "insight" consisted of a decision that "positive action" was the key to interpersonal relations. When first seen (predrug interview), he was characterized by an excessive desire to please and an anxious ingratiating manner. In the interview he was depressed and anxious over his inability to establish himself in peer groups and showed constant preoccupation with the possibility of acquaintances not liking him. As an example of his difficulties he gave his inability to take any side of

* The fact that many subjects would respond to perceptual alterations and unusual bodily sensations with anxiety is not strange since experimental studies have demonstrated a similar reaction when external cues to depth or distance are altered or made ambiguous.[21]

an issue under discussion for fear of offending one or the other side. Under lysergic acid diethylamide he was frightened by a feeling of waning contact with reality and doubts of the presence of objects. This was mitigated by self-reassuring statements and positive assertions: "That *is* the chair," "The doctor *is* here," and so on. The effectiveness of this restitutive activity was so anxiety-reducing that the subject suddenly saw it as a key to adjustment and happiness. On return to college he put "positive assertion" into action with friends, girls, classes, and the like, and two months later reported himself to be "successful and happy" in everything he had undertaken. Unfortunately, restitutive activity is rarely so effective.

A basic question is whether drugs create something new in the organism or only release that which is already present. In previous study of other drugs[19] we have been impressed with the apparent meaningfulness of the atypical drug reaction in terms of the individual's personality structure and current personal problems. The small sample and the diversity of response to lysergic acid diethylamide and lysergic acid ethylamide obscure such a relationship if it exists here, but the Rorschach changes are suggestive.

Lysergic acid diethylamide has produced greater and more profound changes in the results of Rorschach testing than any other drug we have studied. These changes are not striking conversions of normal to psychotic, but rather consistent expansive exaggerations of the predrug personality in which structural weaknesses and immature factors are magnified. In some individuals already characterized by pathologic signs, such a process may produce a "psychotic" picture. The process itself is better viewed, we believe, as a release of existing tendencies rather than a creation of new elements.

Problems of control and design are especially difficult in drug experimentation, not to speak of "experimental psychiatry," and the ideal is rarely achieved. However, the use of subjects as free as possible of bias and suggestion, of vested interest, is essential. The use as subjects of laboratory staff, doctors, and nurses and others sophisticated as to drugs, especially when the experimental drug is known, may lead to erroneous conclusions. This problem was illustrated by one of the lysergic acid diethylamide volunteers whose visual "hallucinations" were remarkably similar to those of another earlier subject. Striking similarity of personality structure and especially of major personal problems of the two provoked much interest. This interest was greatly lessened, however, when it was discovered that he was the earlier subject's roommate and had discussed in detail his friend's drug reactions before volunteering.

SUMMARY

The reactions of the 10 young healthy male subjects to lysergic acid diethylamide and 9 similar volunteers to lysergic acid ethylamide are described and related to the personality of the subjects. Psychologic interview plus the Rorschach Psychodiagnostic Test were given to all subjects before drug administration and repeated during the height of the reaction to lysergic acid diethylamide. The drugs were administered as unknowns. The following observations were made:

Lysergic Acid Diethylamide

1. Changes in vital signs were of slight moment. Giddiness, tremulousness, and paresthesias were frequent.
2. Mood changes included, commonly, tension or anxiety and desire to laugh without normal cause. Less frequently euphoria and erotic sensations were encountered.
3. Thought and speech processes were slowed down and efficiency impaired.
4. Perceptual changes or visual illusions were produced in half the subjects.
5. Seven of the 10 subjects showed distinctive changes in the postdrug Rorschach, taking the form of an exaggerated caricature of the predrug state in which weaknesses of ego function were further undermined.
6. The degree of Rorschach change, as well as the amount of reaction to the drug, was correlated positively with personality disturbances or maladjustment.

Lysergic Acid Ethylamide

1. Transient hypertension, tachycardia, and tachypnea suggestive of epinephrine release were frequent, as well as paresthesias, dizziness, and nausea.
2. Mental changes were predominantly experienced as dulling of the senses, confusion, shakiness, and apprehension.
3. Four of the 9 subjects became mildly hostile and paranoid. One other experienced acute panic.
4. As with the lysergic acid diethylamide, the degree of drug reaction was positively correlated with personal maladjustment.

The possible usefulness of these drugs in "experimental" psychiatry is discussed.

RESUMEN

Se describen y relatan las reacciones de diez jóvenes del sexo masculino a la dietil-amida del ácido lisérgico (DAL) y de nueve voluntarios del mismo tipo a la etilamida del ácido lisérgico (EAL). Antes de la administración de la droga se hicieron exámenes psicológicos y la prueba del psicodiagnóstico de Rorschach, a todos los jóvenes, repitiéndose los exámenes y la prueba durante el período culminante a la reacción del DAL. Las drogas se administraron sin ser identificadas por los individuos objeto de este estudio.

Los resultados obtenidos dieron lugar a las observaciones siguientes:

DAL

1. Los cambios en los signos vitales fueron de escasa duración. Fueron frecuentes el aturdimiento, temblor y parestesias.
2. Los cambios de humor incluyeron comúnmente, la tensión por angustia y los deseos de reir sin causa justificada. Se observaron con menos frecuencia, euforia y sensaciones eróticas.
3. El pensamiento y los procesos de expresión oral se retardaron disminuyendo su eficiencia.
4. En la mitad de los individuos se presentaron alteraciones de la percepción o ilusiones visuales.

5. Siete de los diez mostraron cambios apreciables en el Rorschach realizado después de la administración de la droga, adoptando la forma de una caricatura exagerada comparados con su estado anterior a la ingestión de la droga, en el cual las funciones debilitadas del yo estaban además alteradas.
6. El grado del cambio del Rorschach, así como el de la reacción a la droga, estaban positivamente correlacionados con los trastornos de la personalidad o desadaptación.

EAL

1. Fueron frecuentes la hipertensión, taquicardia y taquipnea transitorias que sugirieron la liberación de adrenalina, así como las parestesias, vértigos y náuseas.
2. Los cambios mentales predominantes fueron el embotamiento de los sentidos, confusión, agitación y aprehensión.
3. Cuatro de los nueve sujetos se hicieron ligeramente agresivos y paranoicos. Otro experimentó un pánico agudo.
4. Al igual que ocurrió con el DAL, el grado de reacción a la droga estaba positivamente correlacionado con la desadaptación personal.

Se discute la posible utilidad de estas drogas en la psiquiatría "experimental."

RESUME

Les réactions des dix jeunes hommes sains à l'acide lysergique diéthyle amidé et les réactions de neuf volontaires semblables à l'acide lysergique éthyle amidé sont décrites et liées à la personnalité des sujets. Un interview psychologique ainsi que le test psychodiagnostique de Rorschach furent donnés à tous les sujets avant l'administration de la drogue et répétés au point maximum de la réaction à l'acide lysergique diéthyle amidé. Les drogues furent administrées comme inconnues. Les observations suivantes ont été faites:

Acide lysergique diéthyle amidé

(1) Les changements en signes vitaux furent peu importants. L'étourdissement, le tremblement et la paresthésie furent fréquents.
(2) Les changements d'humeur comprenaient généralement la tension ou l'anxiété, et l'envie de rire sans raison. Et moins fréquemment l'euphorie et des sensations érotiques.
(3) La faculté de penser et de parler ralentit et la capacité de bon fonctionnement diminua.
(4) Des changements de la perception ou illusions visuelles se manifestèrent chez la moitié des sujets.
(5) Sept des dix sujets ont accusé des changements distincts au test de Rorschach donné après la drogue, prenant la forme d'une caricature exagérée de l'état avant l'administration de la drogue, au cours desquels la diminution de la fonction de l'égo était détériorée davantage.
(6) Le degré du changement au test de Rorschach, ainsi que le degré de réaction à la drogue étaient liés positivement aux troubles et au déréglage de la personnalité.

Acide lysergique éthyle amidé

(1) L'hypertension temporaire, la tachycardie et la tachypnée rappelant l'effet de

l'adrénaline étaient fréquentes, ainsi que la paresthésie, l'étourdissement et la nausée.

(2) Les changements mentaux se manifestèrent surtout par l'abrutissement des sens, la confusion, le tremblement et l'appréhension.

(3) Quatre des neufs sujets devinrent légèrement hostile et paranoïde. Un autre éprouva une panique sévère.

(4) Tout comme avec l'acide lysergique diéthyle amidé, le degré de réaction à la drogue était en corrélation positive avec le déréglage de la personnalité.

On traite de l'utilité possible de ces drogues en psychiâtrie expérimentale.

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