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From the Department of Psychiatry, University of Manchester, England
(Prof. E. W. Anderson)

Clinical Studies of Lysergic Acid Diethylamide

By E. W. ANDERSON and K. RAWNSLEY

This paper deals with the effect of lysergic acid diethylamide (L.S.D.) on a group of normal volunteers and psychiatric patients. The publication of these observations was undertaken for the following reasons:—

(a) the wide range of dosage employed, viz., 10–600 microgrammes (γ)

(b) the occurrence of phenomena either not previously reported in the literature or else not emphasised

(c) continuous administration over days of the substance in some instances

(d) modification of the clinical state of a more lasting character in certain cases

(e) the illumination of basic personality structure in a limited number of cases.

In the course of this study L.S.D. was given to 23 subjects (4 normal volunteers, 3 men, 1 woman, all members of the staff of the department, and 19 patients) involving a total of 58 administrations.

Psychiatric patients.

Diagnostic category	Number of patients
Anankastic disorder	5
Hysteria, including 1 case of psychogenic amnesia	4
Sensitive paranoid reaction	3
Schizophrenia	5
Endogenous depression	2

Sex:— 14 females; 5 males. Age range:— 21–49 years.
The greatest number of administrations to a single patient was 16.

Method. The drug was supplied in ampoules containing 100 γ/ml aqueous solution and was administered in all cases by mouth to fasting subjects. Administration was commenced as a rule at 10.00 a.m. except in a few cases where it was given in the early afternoon for convenience. Each subject was kept under continuous psychiatric supervision over the period of acute intoxication and for a variable period afterwards in certain cases.

During the intoxication the *Rorschach* and *Bender Gestalt* tests were administered.

An electroencephalogram was recorded in 8 subjects.

Observations on the glucose tolerance curve were made during the intoxication in 6 subjects (9 estimations in all).

Patients were confined to bed for the period of clinical observation; normal subjects generally remained seated though were allowed to walk about in the department. No attempt was made to darken the observation room at any time.

Results and Discussion.

A. Clinical. Symptoms of intoxication appeared between 15 and 60 minutes following administration and a maximum effect was attained between 105 and 230 minutes from the commencement. The effects subsided rather gradually and in many instances were present until the subject fell asleep the same evening.

Clinical observations were in the main confined to the psychological aspects of the intoxication and no attempt was made to assess the neurological status or other changes at a physiological level (apart from E.E.G. and glucose tolerance).

The psychological disturbances are presented for convenience under headings. At the end of each section special points are commented upon and the results are discussed in relation to those of other authors.

1. Visual disturbances occurred in 15 subjects.

Undulation of outlines or of surfaces was the most frequent phenomenon, variously described as "seeing from behind a watchman's fire" or "wavering". Distortion of perspective was also common, the room appearing "on a slant" with fixtures projecting from walls and ceiling at apparently disproportionate angles.

Colour vision was disturbed in a few cases and the changes include the production of a striking luminous quality in existing colours, and in one instance a rhythmical variation in general colouring from "bright and cheerful" to "drab and dreary", coincident with a mood change.

Among other visual manifestations occurring in isolated cases may be mentioned transient blurring, flicker at the periphery of the visual field, and synaesthesiae provoked by sounds.

Hallucinations other than an occasional simple flash of light were absent. Illusionary misinterpretations occurred in 2 cases.

In agreement with *Becker*, *Liddell* and *Weil-Malherbe*, and *Condrau*, complex visual hallucinations did not occur, and in general even elementary visual hallucinations were the exception rather than the rule. It should be noted however that our experiments were carried out in a lighted room, though *Condrau* observed no difference in his subjects between a lighted and a dark room.

The rhythmical variation in colour perception noted in one case directly related to spontaneous fluctuations of mood was also observed by *Stoll* in a single case.

Synaesthesiae as reported by *Stoll* and others occurred in only 1 case.

2. Auditory phenomena were noted in 8 subjects.

The commonest effect was a general hyperacusis occurring in 6 subjects. An auditory hallucination consisting of transient music

"like a harp" was reported following the administration of 600 γ. Reverberation of sounds occurred in one instance.

Hyperacusis has been noted by several workers. Hallucinations of music are rare: *Becker* reports one instance of this.

3. *Cutaneous sensation* was modified in 8 subjects.

Paraesthesiae of the face, notably in the circumoral region and of the limbs were common. The sensations were reported as tingling, numbness or burning. One (normal) subject noted a recrudescence of tingling in the left thumb previously experienced several weeks earlier in relation to a minor trauma to radial nerve branches at the wrist.

This return to consciousness for a short time of an organically determined symptom during the intoxication is noteworthy and may suggest a physiological basis for certain hypochondriacal symptoms in mental illness, which emerge whenever the threshold of perception falls—in *Janet*'s phrase, whenever a lowering of the niveau of psychic tension occurs.

4. *Taste* was affected in 6 subjects.

A "metallic" taste or an indescribable "unpleasant" flavour was reported. In one instance, during ingestion of a meal, the various flavours were experienced quite separately and refused to blend in any way. Also each individual flavour had a coarse "essence" quality about it.

The separation of flavours thus described is probably a further instance of "dedifferentiation" which can show itself in all spheres, as, for example, in a case of *Becker*'s where all auditory stimuli had the same value as those of the observer's voice in a conversation with the patient.

The "coarsening" of flavours in the same subject is possibly akin to a coarseness of colour perception noted in one of *Stoll*'s cases.

These phenomena may well depend in part on individual physiological variations.

In agreement with the majority of observers, hallucinations of taste and smell were not reported.

5. *Space perception* was disturbed in 13 cases.

10 subjects experienced a curious sense of spatial insularity in which their immediate environment seemed entirely detached from

its wider setting. Thus some spoke of being "cut off", the surroundings "remote". While remaining intellectually aware of the existence of the outside world, everything without the four walls lost all immediacy or relevance.

A few subjects found the room much larger or smaller than initially.

In isolated instances the sense of spatial continuity of various aspects of the room was broken up and on glancing from one side to the other the effect was comparable to two distinct film sequences of the same room, the connexion between the two being implied, but not clearly felt or experienced.

The experience of spatial insularity does not seem to have been reported by other authors. This is an example of limitation of the psychic horizon, a "blinkering", as one of our normal subjects described it. According to this subject it would not be wholly accurate to regard this, in his case at least, as a predominantly cognitive disturbance but rather one more of affect and ego-function. The sense of participation in anything outside the four walls was absent.

One patient remarked that the ward seemed larger, and the beds wider apart. Exactly the converse was reported by a patient of *Benedetti* who found the ward constricted and was amazed that people could walk in and out between the beds.

6. Thought disorder was noted in 16 subjects.

A tendency for thoughts to vanish suddenly was the commonest effect. This was reported by different subjects as thoughts "flicking" round the corner", "slipping away", "just vanishing", "flashing in and out". In one instance this phenomenon was definitely dependent upon shifting of attention; thus, if, while considering some proposition, the gaze lighted upon a particular object in the environment, the field of attention became wholly and exclusively occupied by the percept—it was as if there was no room for both items simultaneously.

Also of frequent occurrence were difficulty in concentration, impairment of grasp and reduction in problem-solving performance (simple problems in mental arithmetic). A difficulty in holding more than a single thought in mind at any one moment rendered virtually impossible the comprehension of complex written or spoken statements in certain cases. The same disturbance promoted extreme distractibility because the attention-field tended to be fully occupied

with whatever percept or image it had chanced upon a moment earlier.

A few subjects complained of being "muddled". Other disturbances occurring in isolated cases include "speeding up" of thoughts, "crowding" (in a hysteric), "rumination" and "loss of control".

The tendency of thoughts to evanescence, commonly reported by schizophrenics, is, in that disorder, invariably accompanied by the characteristic ego-changes and thus the experience differs from the superficially similar symptom occurring in L.S.D. intoxication. Ego changes occur in the latter state (v.i.) but do not combine with the thought disturbance present simultaneously and hence the experience seems to escape a true schizophrenic quality in this respect.

The failure to synthesise, the tendency to apprehend discrete parts rather than the whole, is, of course, characteristic of organic disorders whether chronic, due to a long-standing cerebral lesion, or transitory, as in toxic states. The subjects also showed evidence of *Goldstein*'s "stimulus boundness". Similar disturbances have been noted by others, e.g. *Stoll*, *Becker*, *Condrau* and *De Shon*.

7. *Mood changes* occurred in 23 subjects.

Affective changes were very common indeed throughout the series of administrations. There was no constant pattern of response in that sometimes the drug would intensify the existing affective state, and at other times would provoke the reverse state.

A striking feature was the tendency to spontaneous marked fluctuations of mood during the intoxication as instanced by one subject who oscillated between extreme elation and profound depression within minutes. Also, in some subjects the mood was qualitatively appropriate to the surrounding affective environment, but quantitatively markedly exaggerated.

Anxiety occurred in 12 subjects at some stage in the intoxication. In many cases it was relatively transient and related for example to being left in the room alone or to a disturbing ego-change. In others it was the dominant mood and persisted until the drug effects subsided or were neutralised.

Euphoria and elation taken together were much commoner than depression. Tension was produced in about a third of the subjects, notably among the obsessional group. A sedative and relaxing effect was noticed in others. In three instances the mood "switched" quite suddenly from one level to another which then persisted through-

out the day. Bouts of uncontrollable laughter occurred to a marked extent in one case.

The mood changes were in general similar to those noted particularly by *Stoll*, *Hoch*, *Forrer* and *Goldner*, *De Shon*, *Liddell* and *Weil-Malherbe*, and *Savage*.

A distinct "tranquillising" effect observed in 4 cases has not been emphasised in the previous literature though *Condrau* remarks that in 3 of his patients the mood was neutral, i.e. neither euphoric nor depressed. This state of tranquillity was not associated with any other features of ecstasy.

Sudden and persistent changes in the experience have not been emphasised by other authors. In our material there were three such instances of a rather striking nature. In the first case, a man suffering from sensitive ideas of reference received 200 γ L.S.D. and became moderately depressed. During interrogation 1 ½ hours after taking the drug he suddenly began to chuckle and felt very amused. He remained in a state of mild euphoria for several hours. The same patient on a subsequent occasion was given 400 γ L.S.D. and became euphoric. 3 ½ hours later, lying with his eyes closed, he experienced a sudden "flash of lightning" and became very anxious. The anxiety gradually subsided but he now felt depressed and continued so for the duration of the intoxication. In the second case, a normal woman, the change came towards the end of the intoxication. The dose was 125 γ L.S.D. and the main feature of the resulting intoxication was a severe depersonalisation with a rather flat, neutral affect. 3 ½ hours later, immediately subsequent to a detailed examination of the mental state, there was a sudden "switch" to perfect normality, apparently coinciding with the general easing-up of tension in the room.

8. Sexual excitement was provoked in 8 subjects (1 male, 7 female).

Of these, 3 were in the anankastic category, 3 schizophrenic, 1 hysteric and 1 depressive. The majority of subjects experiencing sexual excitement received a dose of 200-250 γ L.S.D. In one case, however, mild stimulation occurred with 40 γ.

The degree of excitement became extreme, verging upon orgasm in the case of a female anankast. In a schizophrenic male, the sexual excitement formed one component of a mystical experience not wholly pleasant (described more fully under *ego disorder*). A chronically depressed female experienced sexual feeling compounded with anxiety amounting at times to panic, or so it seemed.

The majority of authors found no change in sexuality though an increase of sexual interest was noted in some cases by *Forrer* and *Goldner*. *Liddell* and *Weil-Malherbe* remark that in the euphoric phase the patients occasionally made "erotic advances". *Stoll* expressly states that during L.S.D. intoxication, libido was diminished.

Whether the increase in sexual feeling can be attributed to a direct influence on the centres governing sexuality or whether it is brought about indirectly through mood changes, euphoria or more particularly anxiety, must remain an open question.

9. Paranoid features occurred in 8 subjects.

Accentuation of a schizophrenic paranoid state was found in 2 cases and enhancement of strong ideas of reference took place in 2 sensitive reactions. For the rest, the paranoid attitudes amounted to a state of general suspicion usually of transient duration, e.g. one normal subject felt suspicious and uneasy if two of the observers glanced at each other and he experienced the idea that they were teaming up against him; insight was largely preserved however.

In no case in a normal subject did paranoid ideas or attitudes reach the intensity of that reported by *Condrau* in one of his ostensibly normal subjects. In general our findings corresponded to those of other authors, e.g. *Savage*.

10. A disturbance of ego-experience happened in 15 subjects.

The commonest form of ego-disturbance (occurring in 7 subjects) was a feeling of impending ego-dissolution. This state was usually accompanied by considerable anxiety and was not necessarily associated with the higher doses, occurring in 2 instances after 50 γ L.S.D. In some cases it was provoked by leaving the subject alone in the room for a few minutes, in some during intensive questioning, in one normal subject it arose during a period of frustration when his insistence on the irrelevance of a particular test was ignored, in others it came about spontaneously. Several subjects on recovering from their fear described the feeling as one of "slipping away". A normal subject stated: "The experience became more and more disorganised... not going to sleep... I was being disorganised", and later the same subject describing this state in more detail said: "The world around was really looking very distorted indeed, and the feeling of isolation on the time axis had also reached its zenith. I had just failed to comprehend the meaning of various phrases and proverbs indicating a

breakdown of abstraction in addition to other thought disturbances. Altogether things were pretty rocky so I decided to sit back quietly for a moment and reassure myself by returning to my own private inner world. As soon as I introspected in this manner I felt to my dismay that 'I' myself was somehow disturbed. The central core of the personality, the ego, the sense of personal identity, was itself fluctuating and, for want of a better phrase, dissolving". In this case the dissolution experience was transient, lasting a few seconds only, and was accompanied by moderate anxiety.

Depersonalisation occurred in 6 subjects, sometimes as a transient state, but in one case persisting steadily throughout the intoxication.

An interesting observation in isolated cases was the positive support experienced in the presence of others. One subject said: "If anyone present went out of the room it felt as though I were being deprived of something. I became smaller—definitely felt vulnerable".

A schizophrenic became intensely preoccupied with an inner experience so that it was almost impossible to gain his attention. As the experience subsided he explained that he had in some way felt nearer to the "truth" or "core of things" and had sensed a curious link with the "truth". This experience had a sexual flavour to it and next day the patient was extremely disturbed and spoke of having had "an unlawful experience".

Other ego-changes related in part to positive moods were a sense of "inner expansion", "rejuvenation" and "heightened integration".

No other writers seem to have stressed the peculiar feeling of ego-dissolution noted by two of our normal subjects and 5 patients who reported in similar terms. It may be remarked, however, that *Savage* speaks of "a desperate holding on" in subjects who "find the distortion of reality too threatening and instead of euphoria there is a heightened anxiety". *Becker* speaks of a loss of boundary between ego and non-ego, as if "dissolved", but it is difficult to be sure whether he means a dissolution in the sense of our subjects or whether this was not an ego-disorder of the type familiar in depersonalisation or ecstasy states. *Becker* also remarks that everything seemed to one experimental subject to be sad, senseless and superficial and that he began to wonder why and to what end the various objects in the environment existed, why indeed anything existed. This subject felt the necessity for clinging to social forms, as did one of our normal subjects, even to an exaggerated degree, as a powerful means of maintaining contact with reality. *Becker*'s subject felt that as soon as he lost this

power he would be delivered over to an unknown force which at that very moment would rob him of all will and thought.

The depersonalisation phenomena noted in our cases were essentially similar to those reported by other writers.

The "mystical" experience of our schizophrenic subject has obvious connexions with ecstasy but lacked entirely the typical feeling tone of the ecstasy state, particularly the sense of tranquillity. The feelings of inner expansion, rejuvenation and heightened integration reported by other subjects suggest further links with states of ecstasy and have not been previously reported in this form in the literature.

11. Time disorder was reported in 13 subjects.

The commonest experience was a sense of temporal insularity in which only the present was real, past and future being exceedingly remote. One normal subject said: "Normally if you look back to your immediate past the experiences you have just had are echoing in your present experience, they have a reality feeling about them. The feeling I had was that recent experiences were completely cut off... they had no presence or reality to me at all. The future... no possibility of anticipating what was going to happen—it seemed new in an entirely novel sense; you could not apprehend in any way what it would be like".

Another subject felt himself in "a timeless suspended state". A few subjects felt time to be slipping by very quickly, in others the passage of time was slowed down. In a case where the mood fluctuated between elation and depression the sense of time-passage was respectively rapid and slow.

In general our results correspond with those of other authors, notably *Becker* who devotes a good deal of attention to this disturbance.

A patient in the present series with a chronic depression accompanied by marked ego disorder amounting at times to a *délire de négation* viewed the idea of eternity with abhorrence. During L.S.D. intoxication she became panic-stricken, having experienced a marked sense of timelessness. This is in contrast with one of *Becker*'s subjects who likewise experienced transient anxiety lest the timeless state persist, but she eventually became free from anxiety because she was unable to look ahead and hence could not feel anxious about future events.

12. Changes in body image occurred in 11 subjects.

The most frequent disturbance consisted of a curious feeling of "lightness", so pronounced at times as to create the sensation of floating in mid-air. Also common was the impression of a general diminution in body size. The feeling that a part of the body had increased in size occurred in a few cases, usually in the region of the face or the hands.

In isolated instances, an unawareness of the whole or part of the body was reported and in one case an increased awareness of the body. One subject stated "Nothing belongs to me except my head and chest". In a single case the body was felt to be splitting up: "Arms a speck—about half-an-inch—don't belong to me... not just my legs, my head, all separated—they're floating all over the place!"

Our findings in this sphere do not differ essentially from those of other writers.

13. Symptoms attributed to *autonomic disturbances* were noted in 18 subjects.

Nausea, dizziness and a feeling of warmth were the commonest effects. Less frequent were shivering and chilly sensations, headache, "light-headedness", faintness, sweating and palpitation.

14. Drowsiness occurred in 8 subjects.

This symptom is not stressed by other workers though *Hoch* reported drowsiness in a proportion of cases and *Condrau* mentions tiredness as an occasional finding.

Prolonged after-effects of L.S.D.

In 6 cases changes in the clinical picture following L.S.D. outlasted the period of intoxication.

Two patients in the anankastic group both displaying considerable tension improved following L.S.D. The first patient received a total of 110 γ L.S.D. in 2 doses and the improvement in this case has been maintained for a year. The second patient was given a total of 2050 γ L.S.D. in 11 doses and the subsequent improvement lasted for 6 months followed by a gradual relapse.

A schizophrenic beset by compulsive thoughts was much relieved following a total dosage of 200 γ L.S.D. in 2 doses.

An inadequate psychopath with psychogenic amnesia felt much

better in respect of increased self-confidence and hope for the future following a total of 1500 γ L.S.D. in 4 doses, but the drug did not help in restoring his memory. This patient left the district on discharge and follow-up has not been possible to date.

A patient with sensitive ideas of reference, probably an early schizophrenic, improved for about 3 weeks following L.S.D., thereafter relapsing rapidly; he received a total of 3050 γ L.S.D. in 16 doses.

The remaining case, an involutional depression of long standing, became very agitated during L.S.D. intoxication (single dose of 200 γ) and remained so, together with enhancement of the depressive state, for many weeks, gradually returning to her previous state after this time.

It is clearly not justifiable to draw any definite conclusions as to the long-term action of L.S.D. in modifying the clinical picture from such a small group of patients, more particularly since all those involved were in-patients and hence subject to a host of other environmental changes, but results of this kind have not been reported before.

Effect of large single doses.

600 γ L.S.D. was administered to a man with psychogenic amnesia. A very labile state developed in which the mood fluctuated between aggressive euphoria and agitated depression, with a transient auditory hallucination, body image disturbance, and time disorder.

450 γ L.S.D. administered to the same patient on a previous occasion had an essentially similar effect, though the picture inclined more to depression.

The effect of 400 γ L.S.D. on a patient with sensitive ideas of reference has already been mentioned in discussing sudden and persistent changes in the experience (under *Mood Changes*).

Large single doses (300–500 γ) were also administered by *de Giacomo* to a group of 12 patients, of whom 5 (3 schizophrenics, 2 oligophrenics) passed through a preliminary phase of excitement followed by a typical catatonic state, during which the patient's face remained inexpressive whilst he maintained the same posture for several minutes. This phase lasted up to two hours.

Forrer and *Goldner* administered doses as high as 6 γ/kg body weight to a series of 6 schizophrenics and paid particular attention to the physiological changes.

Stoll considered the question of dosage important in view of *Beringer*'s impression that mescaline in increased dosage does not merely intensify the symptoms but alters them. Such results as *Stoll* obtained with his relatively low dosage did not suggest qualitative alterations of the psychopathological picture with varying doses.

Our findings tend to confirm this view and over a certain minimal dose there is no clear relationship either quantitative or qualitative between the clinical picture and the amount of the substance taken.

B. Psychometric. During the course of the intoxication the *Rorschach* test and the *Bender Motor Gestalt* test were administered. The findings were compared with repeat tests carried out in the resting state. It is not proposed to describe the results of this investigation here as it is hoped that a separate paper by Mr. *J. C. Kenna* will be published in the near future to this end.

C. Electroencephalographic. The E.E.G. was recorded in eight subjects during the intoxication and the tracings were compared with control readings taken in the resting state. An 8-channel *Ediswan* instrument was used and no special method of stimulation was employed other than hyperventilation.

In five instances there was a slight increase in alpha rhythm frequency of between ½ and 2 cycles/sec. In one case the alpha frequency decreased by 1.5 cycles/sec. Other minor non-specific changes occurred in single cases.

DeShon et al. investigated the E.E.G. changes in 9 of their subjects. They found an increase in alpha frequency of 1–3 cycles/sec. in 8 cases and a decrease of 2 cycles/sec. in the remaining case.

Liddell and *Weil-Malherbe* observed no alteration in the E.E.G. and *Forrer* and *Goldner*, employing a dose of 2 γ/kg body weight, likewise detected no change.

D. Biochemical. The effect of L.S.D. on the glucose tolerance test was noted in 6 subjects during 9 administrations of the substance. The technique employed was to estimate the fasting blood sugar at the time of taking the drug and then to administer 50 grams glucose orally one hour later, thereafter taking ½-hourly blood sugars for 2 ½ hours. The values obtained were compared with a control glucose tolerance test carried out under resting conditions.

A detailed analysis of the results was not felt to be justifiable,

but speaking generally the glucose tolerance is slightly diminished during the intoxication, both in regard to higher blood sugar levels at each stage and a rather protracted return to the initial level.

The significance of this finding is impossible to evaluate in view of the presumed secondary effects of L.S.D., such as the mobilisation of adrenaline through affective changes, which in themselves would influence carbohydrate metabolism.

In connexion with these results it may be noted that *Forrer* and *Goldner* observed a slight rise in the fasting blood sugar beginning in the second and third hour of intoxication.

Mayer-Groß et al. in two publications have investigated the effect of L.S.D. on carbohydrate metabolism and, *inter alia*, noted a slight rise in fasting glucose level during the first two hours. From their observations on the action of L.S.D. both *in vitro* and *in vivo* they deduced that the substance exercised a sparing effect on the metabolism of hexosemonophosphate.

Conclusions.

Broadly speaking, the present results confirm those obtained by the majority of previous authors, namely that L.S.D. is a highly active substance producing in very small dosage psychological disturbances of the type familiar in acute toxic states though not involving any considerable clouding of consciousness.

The changes brought about are in the psychic spheres of perception, thinking, mood, sexuality, ego-function (including time-sense) and body image, and also in the vegetative nervous system.

L.S.D. appears to be well tolerated by the organism up to doses of at least 400–600 γ by mouth; at these levels no untoward symptoms were observed which might have heralded collapse.

With regard to phenomena not previously emphasised in the literature we note particularly the production of sexual excitement in rather more than one third of the cases studied. Secondly, the sudden "switch" in the total experience occurring in 3 cases, the change persisting at the new level, is of considerable interest, especially in the single case where the alteration appeared to be related to a change in the emotional climate of the environment (a deliberate easing-up of tension).

Although systematic observations were not undertaken it is our impression that there is a rather complex relationship between the mental state under L.S.D. and the surrounding environment. There

would appear to be scope for further study, perhaps involving the reaction of intoxicated subjects to pre-arranged and carefully structured changes in the surroundings (the subject, of course, being unaware of what was in store for him).

Thirdly, the alarming experience of impending ego-dissolution, occurring in 7 subjects, is noteworthy and illustrates the profound disturbance of central ego-function which L.S.D. may produce.

Finally, attention is drawn to the extremely variable action of L.S.D. in the same subject day by day. On occasions the drug may seem to underscore the clinical picture, e.g. depression may become enhanced, but next day the same dose may elicit a state of euphoria in the self-same patient.

The possible use of L.S.D. as a diagnostic aid has been debated by various authors. Stoll regarded both L.S.D. and mescaline as of very limited value in this connexion. *Becker* likewise did not attach much importance to this aspect of the intoxication but considered it might be of use in determining the formal aspects of a personality as distinct from the content. He cites the case of a female subject who had a reactive affective stupor some years previously and who developed a comparable state during L.S.D. intoxication. *Condrau* remarked that the evaluation of the drug in this respect would entail making a large series of observations. He noted that L.S.D. made catatonics more catatonic, hebephrenics more hebephrenic, and so on. In normal subjects L.S.D. produced a "caricature" of the normal personality.

On the basis of our own results we can state that the observed effects of L.S.D. were of no value in confirming or refuting the clinical diagnosis in any individual case. In some instances, however, the intoxication served to throw into relief particular aspects of the psychosis or psychopathic disturbance, e.g. the patient with a long-standing involutional depression who became very much more agitated and depressed during and for some time after the intoxication.

We were impressed by the illumination of the formal aspects of personality structure in a few cases. Two of our normal subjects, both affectively warm syntonic individuals, developed states of mild elation with a rather boisterous good-humoured element which, in *Condrau*'s sense, certainly provided a caricature of the basic temperament in each instance.

With regard to the therapeutic possibilities of L.S.D. we are unable to draw any firm conclusions from our own material. In this connexion *Stoll* was also unable to judge the therapeutic value of

L.S.D. on his data. *Condrau* administered a daily increasing dose of L.S.D. to 5 depressives and found that 2 patients became more accessible and less retarded. More permanent improvement in the mood, however, beyond a daily fluctuation, did not occur and indeed, on the whole, the patients tended to become more depressed.

Savage gave 15 depressed patients a daily dose of L.S.D. for a month and subsequently followed the cases up for 6 months, comparing their progress with an untreated control group. There was no significant difference between the two groups.

Hoch et al. on the basis of giving L.S.D. in single and in repeated doses to a group of 21 schizophrenics conclude that a therapeutic action does not occur.

Busch and *Johnson* selected 8 patients for psychotherapy under L.S.D. (4 psychoneurotics, 1 psychosomatic, 3 catatonic schizophrenics). They note the development of a "transitory toxic state which disturbed the barrier of repression and permitted a re-examination of significant experiences of the past ... some of the patients were then able to re-evaluate the emotional meaning of some of their symptoms and improved".

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Summary.

d lysergic acid diethylamide has been administered to a group of 4 normal volunteers and 19 psychiatric patients, altogether on 58 occasions. The dose employed ranged from 10–600 γ L.S.D. and was given by mouth.

The cases were studied by direct clinical observation, psychological testing, electroencephalography, and by estimation of the glucose tolerance.

Symptoms appeared within 15–60 minutes of ingestion and were maximal within 105–230 minutes. They comprised perceptual disturbances in the following modalities—visual, auditory, cutaneous, gustatory, and spatial; thought disorder; mood changes; heightened

sexuality; ego-disorders; changes in body image; autonomic disturbances; drowsiness.

In 6 cases L.S.D. was followed by long-lasting changes in the clinical picture.

The organism tolerated high single doses of L.S.D. satisfactorily and the psychological changes were not quantitatively proportional to the amount given.

E.E.G. changes were minimal during the intoxication and in the main comprised a slight increase in alpha frequency.

The glucose tolerance is shown to be somewhat reduced during the intoxication.

Phenomena not emphasised in the previous literature are described and the role of L.S.D. as a diagnostic and therapeutic agent is discussed.

Zusammenfassung.

Lysergsäure-Diaethylamid wurde einer Gruppe von 4 normalen freiwilligen Versuchspersonen und 19 psychiatrisch Kranken gegeben, zusammen in 58 Versuchen. Die Dosis betrug 100–600 γ L.S.D. per os; beobachtet wurde klinisch, mit Hilfe von psychologischen Tests, elektroencephalographisch und durch Messung der Glukosetoleranz.

Es erschienen innerhalb 15–60 Minuten Symptome, in maximaler Ausprägung nach 105 bis 230 Minuten. Sie traten auf in Form von visuellen, akustischen, Haut-, Geschmacks- und räumlichen Störungen; Störungen des Denkens, affektiven Störungen, erhöhter Sexualität, Ichstörungen, Störungen des Körperschemas, vegetativen Störungen, Schwindel.

In 6 Fällen zeigte sich langdauernde Veränderung des klinischen Krankheitsbildes. Es wurden hohe Einzeldosen vertragen, die psychologischen Veränderungen erfolgten nicht proportional der Höhe der Gaben. EEG-Veränderungen waren während der Giftwirkung geringfügig, in der Hauptsache zeigte sich ein leichtes Anwachsen der Alphafrequenz. Die Glukosetoleranz erwies sich leicht vermindert während der Wirkung. Auf Erscheinungen, die in der bisherigen Literatur nicht erwähnt sind, wird hingewiesen, der diagnostische und therapeutische Wert von L.S.D. diskutiert.

Résumé.

L'acide d lysergique diethylamide (L.S.D.) a été administré à un groupe de 4 volontaires normaux et de 19 malades psychiatriques,

à 58 reprises au total. La dose employée allait de 10 à 600 γ L.S.D. et été donnée par voie buccale.

Les cas ont été étudiés par l'observation clinique directe, par les tests psychologiques, par l'électroencéphalographie et par l'estimation de la tolérance au glucose.

Les symptômes faisaient leur apparition 15-60 minutes après ingestion et atteignaient leur maximum dans l'espace de 105–230 minutes. Ils consistaient en perturbations de la perception des modes suivants: visuel, auditif, cutané, gustatif, et spatial; en désordres de la pensée; changements d'humeur; élévation de la sexualité; désordre de l'ego; modifications de l'image corporelle; altérations autonomes; somnolence.

Dans 6 cas, le L.S.D. fut suivi de changements de longue durée de l'image clinique.

L'organisme tolérait de façon satisfaisante de fortes doses uniques de L.S.D. et les modifications psychologiques n'étaient pas proportionnées quantitativement aux doses administrées.

Les modifications de l'E.E.G. se montrèrent minimes pendant l'intoxication et étaient caractérisées surtout par une légère élévation de la fréquence alpha.

La tolérance au glucose s'est montrée quelque peu réduite pendant l'intoxication.

L'auteur décrit des phénomènes non encore relatés dans la littérature antérieure et discute du rôle du L.S.D. en tant qu'agent de diagnostic et de thérapeutique.

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Authors' addresses: Dr. E. W. Anderson and Dr. K. Rawnsley, Department of Psychiatry, University of *Manchester* (England).