Psychopharmacologia (Berl.) 9, 340—346 (1966)

Clinical Prediction of Insightful Response to a Single Large Dose of LSD*

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Received November 26, 1965

Favorable therapeutic effects in patients with poor prognosis, such as chronic alcoholics, have been reported to follow a single treatment session in which a large dose of lysergic acid diethylamide (LSD) was administered (CHWELOS *et al.*, 1959; SHERWOOD *et al.*, 1962). The reports suggest that subsequent improvement of behavior appeared more likely to occur in patients who displayed an insightful reaction during and immediately after the treatment session. The reaction was characterized by heightened awareness of past personal events, relation of these events to their problems, and expression of convincing resolutions to change their behavior in more adaptive directions. This response to LSD, consisting of insight and attitudinal reorientation based upon it, has been considered by SHERWOOD *et al.* (1962) to result from a unique and impressive experience, not unlike a religious conversion, induced by the treatment. They used OSMOND's (1957) term, "psychedelic," to designate the experience. The possibility that effective criteria for selecting patients who will manifest an insightful response to LSD could be used to pick favorable candidates for LSD therapy led to the present study, which was undertaken to determine whether responders could be distinguished clinically from nonresponders. Data comparing effects of LSD and methamphetamine were also obtained.

Methods

Subjects were 20 psychiatric inpatients, ranging in age from 16—36 years (median, 24), of whom 13 were men. All were volunteers; the guardians of those under 21 years old also gave consent. The group was selected to exclude overt psychoses, mental retardation and brain syndromes, and to include an adequate representation of conduct disturban-

* This paper is based upon a thesis submitted by D. C. EGGERT in partial fulfillment of the requirements for the M. S. in Psychiatry, University of Iowa, August, 1965.

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ces; half were court referred or had some legal problem related to psychiatric contact. The structured interview used by SMALL *et al.* (1964) was employed for clinical evaluation. All responses to standard questions were recorded verbatim on a protocol sheet; these were then used to complete a checklist of diagnostic criteria, which led to classification according to predetermined rules. The classification differs somewhat from that of the American Psychiatric Association, e.g., the categories include psychopathic personality, but not the varieties of personality trait and pattern disturbances. However, it has the advantages of reasonable reliability and reduction of variability in diagnostic labelling. Diagnoses of the patients obtained by this method were: psychopathic personality, nine cases; exogenous depression, five; psychoneurotic reaction, four; schizophrenic reaction, one; no diagnosis, one. The patient diagnosed as schizophrenic reaction was not, at the time, obviously psychotic. No patients received drugs for at least 38 hrs before test injections; only five gave a history of previous medications for their present condition.

LSD was administered intravenously in a dose of 2.5 mcg/kg body weight; this dose is in the range considered effective by most investigators. Methamphetamine, 20 mg, was also given intravenously to 12 patients of the same group on another occassion; interval between injections was at least 3 days and the order of LSD and methamphetamine was alternated. LSD was given intravenously in order to speed its action, reduce variability of response due to absorption differences, and allow comparison with intravenous methamphetamine.

Preparation for the drug sessions consisted of at least 6 interview hours over a 7—14 day period. In these, current problems were explored, and subjects were prepared for the drug experiences in the manner suggested by CHANDLER and HARTMAN(1960). In general, they were both encouraged to anticipate unusual and important experiences and reassured about these. The drug sessions were conducted much like those described by BALL and ARMSTRONG (1961), except that music was not played and Thematic Apperception Test cards were occasionally used, instead of photographs of relatives, to stimulate verbalization. Sessions were in the office of the investigator, who administered the drug and stayed with the patient almost continuously from 9:00 a.m. until evening. The patient generally reclined on a couch, but could move about if he wished. The investigator attempted to maintain a supportive, interested, and generally nondirective attitude; occasionally he would summarize and review the patient's verbal productions. At bedtime, chlorpromazine, 25—50 mg, was given after LSD, or pentobarbital, 200 mg, after methamphetamine.

The Bender-Gestalt Test and Jarvik Questionnaire (JARVIK *et al.*, 1955) were administered before drug sessions and when drug effects

seemed maximal, i.e., about 30 min after methamphetamine and 60 to 90 min after LSD injection. About 60—90 min of each drug session was tape recorded for rating purposes. Samples were recorded in relation to phasing of verbal productivity. A representative tape covering a 6 hr LSD session, would contain three 2 min samples for the first 90 min period, three 5 min and three 10 min samples for the second and third 90 min, respectively, and two 15 min samples for the fourth 90 min. For methamphetamine interviews, a representative tape would contain eight 10 min samples about evenly spaced over a 4 hr period. In addition, a brief interview conducted 72 hrs after the drug session was fully recorded. The tapes were rated independently by two psychiatrists, each of whom had taken LSD some years before, and who were not otherwise connected with this study. Parenthetically, neither of the authors has taken LSD. The raters had available full routine case material about each patient, but not the structured interview data. They were required to rate each LSD session on a scale from zero to +++. A + rating was given to a session in which self-examination and some insight occurred. In a ++ interview there was reliving of forgotten childhood experience or recall of infantile fantasies, with integration of this material. A +++ rating was given to sessions in which the integrate experience led to realistic self-acceptance with a resolution to improve.

Ratings for LSD sessions were the same in 11 of 20 cases and within one point in 18 of 20. However, the preponderance of zero ratings produced a skewed distribution. This, together with the small number of cases, led us to divide the subject into two groups: eight responders, with a mean rating of 1.0 or more, and 12 nonresponders with a mean rating of 0.5 or less.

Results

Comparison of Methamphetamine and LSD Effects

Methamphetamine interviews were discontinued after 12 patients had been tested because it became apparent that methamphetamine and LSD effects were clearly different. They could easily be distinguished by clinical observation, and by test scores. Mean Jarvik Questionnaire scores increased by only 1.8 points with methamphetamine, compared to 20.6 points with LSD, a highly significant difference (t, 7.51; $p < .001$). Since the questionnaire was designed to bring out LSD effects, this result is not unexpected. Mean Bender-Gestalt scores, determined by the PASCAL and SUTTELL (1951) method, increased (impairment) by 29.9 points with LSD, and decreased 4.9 points with methamphetamine (t, 3.74; $p < .01$). Also, one of the raters was asked to distinguish randomly selected 5 min samples of tape recording with each drug; he was correct 21 of 24 times.

Since the raters could readily determine which drug had been administered insightful response to methamphetamine was not rated.

Correlates of Insightful Response to LSD

LSD responders and nonresponders were compared with respect to: individual traits elicited in the structured interview, diagnostic classification, age, sex, education, and Jarvik and Bender-Gestalt test findings. Fisher's Exact Probability Test (two-tailed) was used in statistical evaluation of data other than test scores (SIEGEL, 1956). Only two traits elicited by interview were differentiative at the .05 level. These were "poor marital history" and "lack of guilt feelings", which occurred more often in responders. However, diagnostic classification of seven of eight responders was psychopathic personality, while only 2 of 12 nonresponders had this diagnosis; the difference was significant ($p < .01$). The other responder was classed as exogenous depression. With respect to age, the data suggested that responders were older than nonresponders. The two nonresponders with psychopathic personality were aged 19 and 20; none of the six patients under 22 were responders, compared to eight of the 14 who were 22 or older. Responders were also predominantly male (seven of eight patients), but this may be due to the fact that there was only one female in the psychopathic personality group. No other findings were differentiative with respect to LSD response.

These data suggest that a single 2.5 mcg/kg dose of LSD is more likely to elicit an insightful response in adult patients in whom psychopathic personality characteristics are predominant. A diagnosis of psychopathic personality required presence of at least five of the following criteria: poor work history, use of aliases, destruction of property, impulsive behavior, sexual promiscuity or perversion, repeated arrests, poor military record, receipt of public assistance, vagrancy, aggression against people, poor school record, poor marital history, excessive use of drugs, pathological lying, lack of guilt feelings. Although the responders showed only two of these individual items significantly more frequently than nonresponders, they more often combined five or more.

Illustrative Case Summaries

Case 1. Responder, rating 2.0. Male, 24. Referred after mishandling insurance company funds and writing bad checks to the amount of $5,000. His parents paid back the money. Poor work history. Wife wanted divorce if he could not be helped, as he was using the money for numerous extramarital affairs. Classed as psychopathic personality. After LSD, 160 mcg, he displayed intermittent laughing and crying, restlessness and agitation for over 2 hrs. Then talked about his failure to use his opportunities, and guilt feelings about his treatment of his

family. Intermittently he reported visual images of cats and leopards, which he related to the feline nature of women. He then expressed the decision to confront his problems, and later stated that he felt entirely different about people, saying he must stop viewing women only as sexual objects. Upon return home, with no further therapy, he worked steadily, got into no trouble, and was regarded as a changed man by his wife and family, for about 7 months. He then began to stay out nights, but returned to the hospital for a second LSD session, with renewed beneficial results.

Case 2. Nonresponder, rating 0.0. Male, 28. Self-referred because of marital problems, reckless driving, unconcern about gambling losses and lack of spiritual values. Responses to structured interview yielded no psychiatric diagnosis. Employed as a statistician. In response to 200 mcg LSD complained of no unpleasant symptoms, but reported visual perceptual changes in detail. Later stated that the experience had no special effect, except to cause him to concentrate upon his problems for a long period of time. He felt it had been unnecessary and that he needed no further psychiatric attention. No follow-up data are available.

Discussion

Present findings suggest that the quality of response to a single large dose of LSD may be predicted from a structured psychiatric interview and that an insightful response is more likely to occur in patients with a constellation of behavioral problems leading to a diagnosis of psychopathic personality. The small size of the sample invites caution in generalizing the findings to all types of psychopaths. The psychopathology of our two nonresponder psychopaths was certainly no less typical than that of the responders. It may be relevant, however, that they were under 21 years of age and that in our experience, we have not so far observed an insightful response in anyone under 21. Age reflects degree of maturity and also the opportunity to develop personality assets. It may be that the extent of personality assets is an important determinant of the quality of LSD response. Should this be so, one might expect less insightful response in chronologically mature psychopaths with few personality assets.

Although the relationship between personality structure and insightful response is of interest, the clinical importance of the results would depend upon the possibility that subsequent therapeutic effects can be forecast by a prediction of the immediate LSD response. As our results with methamphetamine indicate, double-blind methods are virtually impossible with high doses of LSD so that meaningful follow-up data can only be obtained by comparing treated and untreated groups. We are currently analyzing the results of a follow-up study for the present sample of LSD patients and a comparison group matched for age, sex, and symp-

toms. The results so far suggest that favorable behavioral changes occurred more frequently in the patients treated with LSD and that, within the LSD group, the responders did better than the nonresponders. Valid criteria for predicting LSD response may thus acquire practical clinical value.

Therapeutic procedures employing LSD have differed greatly in dosage and number of treatments given. It is possible that our finding that psychopaths are particularly likely to give an insightful response may be true only for a single large dose. In recent experiments with treatment programs involving two to four such LSD injections at weekly intervals, we have found that, while psychopathic personalities are more likely to respond with insight to the first of a series, other types of patients may respond similarly to later injections. It would not be unreasonable to suppose that different kinds of patients may require different LSD regimens for favorable effect. For example, it could be that psychopaths respond better to a few large doses while psychoneurotics require multiple treatments at lower dosage levels. Although this is in accord with actual experience (O'REILLY and REICH, 1962; CHANDLER and HARTMAN, 1960), systematic data are lacking and further investigation is required. The tendency to relapse about 6 months after immediate dramatic behavioral improvement, as seen in Case 1, also invites further study, as our follow-up data indicate that this phenomenon is common.

Summary

Twenty psychiatric inpatients were given a single 2.5 mcg/kg intravenous dose of LSD in the context of a prolonged interview session after preliminary clinical study and indoctrination. Insightful responses, as rated from tape recordings, were found more frequently in patients with characteristics of psychopathic personality than in other types of patients. No responders were less than 22 years of age. A attempt to use methamphetamine as a comparison drug showed that it was easily distinguishable from LSD by clinical observation, Jarvik Questionnaire and Bender-Gestalt score changes, and from randomly selected brief samples of tape recorded verbalization.

Acknowledgment. We are grateful to Sandoz Pharmaceuticals for supplying the LSD, to Drs. JOHN CLANCY and JAY HEINER for their assistance in ratings, to Drs. I. F. and J. G. SMALL for the structured interview schedule, and to the clinical staff of Psychopathic Hospital, Iowa City, for their coöperation in referral and care of patients.

References

BALL, J. R., and J. J. ARMSTRONG: The use of L.S.D. 25 (d-lysergic acid diethylamide) in the treatment of sexual perversions. Canad. psychiat. Ass. J. **6**, 231—235 (1961).

Chandler, A. L., and M. A. Hartman: Lysergic acid diethylamide (LSD-25) as a facilitating agent in psychotherapy. Arch. gen. Psychiat. **2**, 286—299 (1960).

Chwelos, N., D. B. Blewett, C. M. Smith, and A. Hoffer: Use of d-lysergic acid diethylamide in the treatment of alcoholism. Quart. J. Stud. Alcohol **20**, 577—590 (1959).

Jarvik, M. D., H. A. Abramson, and M. W. Hirsch: Comparative subjective effects of seven drugs including lysergic acid diethylamide (LSD-25). J. abnorm. soc. Psychol. **51**, 657—668 (1955).

O'Reilly, P. O., and G. Reich: Lysergic acid and the alcoholic. Dis. nerv. Syst. **23**, 331—334 (1962).

Osmond, H.: A review of the clinical effects of psychotomimetic agents. Ann. N.Y. Acad. Sci. **66**, 418—434 (1957).

Pascal, G. R., and B. J. Suttell: The Bender-Gestalt Test: Quantification and Validity for Adults. New York: Grune and Stratton 1951.

Sherwood, J. N., M. J. Stolaroff, and W. W. Harman: The psychedelic experience—a new concept in psychotherapy. J. Neuropsychiat. **4**, 69—80 (1962).

Siegel, S.: Non-Parametric Statistics for the Behavioral Sciences. New York: McGraw Hill 1956.

Small, I. F., J. G. Small, C. R. Gonzalez, and M. D. Gynther: Content reliability of a structured psychiatric interview. Arch. gen. Psychiat. **11**, 192—196 (1964).

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