Int. Pharmacopsychiat. *8:* 104–115 (1973)

DPT as an Adjunct in Psychotherapy of Alcoholics

S. Grof[1], *R.A. Soskin*[2], *W.A. Richards*[3] *and A.A. Kurland*[4]

Abstract. The usefulness of dipropyltryptamine (DPT) as an adjunct to psychedelic therapy was explored in a pilot study carried out on 51 alcoholic patients from the Alcoholic Rehabilitation Unit at Spring Grove State Hospital. The evaluation of the results was based on the comparison of pre- and posttreatment results of a battery of psychological tests and of pretreatment and follow-up ratings of an independent team of social workers. The psychological tests involved the Minnesota multiphasic personality inventory (MMPI), Personal orientation inventory (POI), Raven progressive matrices, Psychiatric evaluation profile (PEP), and Benton visual retention test. The social history questionnaire used by the social workers for assessment of the patients' adjustment consisted of 0–10-point scales measuring residential, occupational and interpersonal adjustment, abstinence, and global adjustment.

A dramatic improvement was observed on a variety of psychological test variables; in many of them the pre- and postdifferences reached a high level of statistical significance. From a total of 51 patients included in the study, 47 (92.1 %) could be located for follow-up assessment. In this follow-up a statistically significant improvement was found in all the measured parameters of the social history questionnaire. The pretreatment to follow-up differences on the scales of interpersonal adjustment, abstinence and global adjustment reached a high degree of statistical significance ($p < 0.001$). A high rating of more than 8 on the 10-point scales measuring global adjustment and drinking behavior was considered an indicator of 'essential rehabilitation'. On the basis of this definition, the number of 'essentially rehabilitated' patients was 22 (46.8 %) in regard to global adjustment, and 25 (53.2 %) in regard to abstinence. A total of 18 patients (38.2 %) remained completely abstinent for the entire 6-month follow-up period.

1 Chief of Psychiatric Research, Maryland Psychiatric Research Center, Box 3235, Baltimore, MD 21228; Assistant Professor of Psychiatry, Department of Psychiatry and Behavioral Sciences, The Johns Hopkins University School of Medicine, Baltimore, Md.

2 Chief of Psychological Research, Maryland Psychiatric Research Center, Box 3235, Baltimore, MD 21228.

3 Research Fellow, Maryland Psychiatric Research Center, Box 3235, Baltimore, MD 21228.

4 Director, Maryland Psychiatric Research Center and Assistant Commissioner for Research, Maryland Department of Health and Mental Hygiene, Box 3235, Baltimore, MD 21228.

The results seem to justify a controlled clinical study of the therapeutic potential of DPT as an adjunct to psychedelic peak therapy in alcoholic patients. In addition, this substance appears to be promising for use in psycholytic therapy, possibly even on an outpatient basis.

Introduction

Several independent clinical studies carried out during the last decade in Canada and the United States indicated that psychedelic therapy utilizing LSD might be an important contribution to the treatment of alcoholism (1, 2, 7, 9, 11). Carefully designed controlled studies examining this issue have demonstrated that LSD does not have therapeutic value when used predominantly as a psychopharmacological agent within the framework of chemotherapy (5, 8), but that its use as an adjunct to psychotherapy can yield important clinical results (6, 10).

Table I. Percentage of alcoholic patients essentially rehabilitated after LSD treatment[1]

		6 months, %	12 months, %	18 months, %
Global adjustment	high-dose group (450 μg)	44 (28/64)	46 (27/59)	53 (30/57)
	low-dose group (50 μg)	25 (10/40)	34 (12/35)	41 (14/34)
Drinking behavior	high-dose group (450 μg)	53 (34/64)	47 (28/59)	54 (31/57)
	low-dose group (50 μg)	33 (13/40)	48 (17/35)	47 (16/34)

1 Scores of 8, 9, or 10 on a 0–10 rating scale.

An extensive series of controlled clinical studies relative to the usefulness of LSD-assisted psychotherapy in various psychiatric disorders has been in progress over the past 10 years. In one of these studies, 135 alcoholic patients were randomly assigned to a high-dose treatment group (450 μg of LSD) or a low-dose control group (50 μg of LSD). Significant improvement was observed in both groups from pre- to posttreatment on a variety of psychological test variables. The follow-up in this study was carried out by an independent evaluation team at 6, 12 and 18 months after the termination of the LSD treatment. A marked clinical improvement was observed in a large proportion of the patients in both groups during all three follow-up periods (table I) (6, 10).

The results of these studies suggested new possibilities in the treatment of

alcoholism. A concentrated and systematic effort on the basis of this data has been dedicated to the study of various variables of the psychedelic treatment process, with the final goal of increasing its efficacy and safety. An important part of these efforts has been the search for a psychoactive drug with similar effects as LSD but without some of its drawbacks and disadvantages, such as long duration of its effect and prolonged termination period of the sessions characterized by wavelike episodic recurrence of an altered state of consciousness.

Appreciation of the therapeutic potential of LSD on the one hand, and awareness of the mentioned drawbacks and limitations on the other, logically resulted in a search for a psychoactive drug with therapeutic efficacy superior or at least comparable to LSD, but with a shorter period of action and possibly more abrupt return to normal consciousness.

A review of the literature on psychoactive drugs for a substance with the aforementioned properties drew our attention to the group of tryptamine derivatives. The pioneering research in the area of study of this interesting and theoretically important group of substances was done by *Szara* (12–14, 16), *Szara et al.* (15) and *Vourlekis et al.* (17). Pursuing research in the direction outlined by the adrenaline hypothesis of schizophrenia as formulated by *Osmond, Hoffer* and *Smythies, Szara* focused his attention on alkylated tryptamine derivatives and the metabolism of tryptophane. He became first interested in the possibility of hallucinogenic action of alkylated tryptamine derivatives in 1955, after learning about the chemical analysis of cohoba, a snuff powder prepared from *Piptadenia peregrina* seeds, which the Haitian natives use in religious ceremonies to produce mystical states of mind and to communicate with their gods. From a total of 13 tryptamine derivatives synthesized by *Szara* and tested clinically, only dimethyltryptamine (DMT), diethyltryptamine (DET) and dipropyltryptamine (DPT) proved to have hallucinogenic properties in experimental subjects (3, 15, 16). Other closely related derivatives, such as dibutyl-, dihexyl- and 6-fluoro-DET were not hallucinogenic (4, 16).

According to the data in the literature, DMT and DET seemed to have unpleasant autonomic and visceral side effects, and the duration of their action appeared to be too short for therapeutic utilization. The next higher homologue, DPT, seemed to be a much more promising candidate; *Szara*'s preliminary data suggested that DPT produces qualitatively the same effects as LSD and may 'effectively and conveniently replace the much longer acting LSD-25' (14).

These observations were encouraging enough to justify a systematic investigation of the therapeutic potential of DPT in alcoholic patients. After the completion of a small pilot study in which we became acquainted with the effects of DPT and obtained the necessary basic clinical experience with this compound, we started a larger exploratory study of its therapeutic potential in alcoholic patients, which is the object of this presentation.

Present Study

Methodology

Selection of the Patients and Description of the Sample

This exploratory study of the therapeutic potential of DPT was carried out in a group of 51 alcoholic patients selected from the patient population in the Alcoholic Rehabilitation Unit (ARU) of the Spring Grove State Hospital on the basis of their appropriateness for psychedelic-peak therapy. After physical and psychiatric examination, the psychiatrist in charge of the alcoholic unit recommended possible candidates for the research program. Patients with organic brain damage, epilepsy, active kidney or liver disease, severe cardiovascular disorders and overt psychotic disturbances were immediately excluded from further consideration. The referred patients were interviewed by a member of the Maryland Psychiatric Research Center who determined their willingness to participate in the experimental treatment program and asked for a commitment to remain in the hospital for the estimated 4–6 weeks. After the screening interview, the patients were referred for a battery of pretreatment psychological tests, and a social history was taken by a social worker. The selection of the patients for the experimental treatment program was based on consideration of the contraindications alone; no patient was excluded because of the severity of the drinking problem or an estimate of poor clinical prognosis.

Of the 51 patients, 13 were married, 10 single, 11 separated, 15 divorced and 2 widowed. The age range was 27–60 years; the average age 38.6 years. 42 patients were Caucasian, 8 were Negro and 1 was half Indian and half Negro. 31 of the patients completed high school; the occupations of the patients covered a wide range from a minister through clerks and salesmen, to skilled workers and unskilled laborers.

The duration of the drinking problem ranged from 2–25 years, with an average of 10.4 years. The number of previous state hospital admissions was 0–6 (average 1.9).

Therapeutic Procedure

The treatment procedure employed in the DPT study was essentially the same as the therapeutic approach employed in previous studies. The basic principles of this method have been described in detail elsewhere (10). It consists of three mutually interrelated phases: (1) a series of drug-free interviews in which the patient is being prepared for the drug session, (2) the DPT session(s), and (3) several subsequent drug-free interviews for the integration of the session(s).

The preparation lasted usually 12–15 h, extended over a period of 2 or 3 weeks. During this time, the therapist and the patient discussed in detail the patient's life history, searching for pathogenic influences and trying to under-

stand the basic psychodynamics and the mechanism of the drinking pattern. The preparation also involved discussion of the patient's religious beliefs, basic life philosophy and hierarchy of values. Since a good therapeutic relationship and atmosphere of basic trust seem to be the single most important variable of successful psychedelic therapy, much effort was exerted to establish a sufficient closeness of rapport and to provide the quality of a real human encounter. When the therapist felt that the goals of the preparation had been accomplished, he scheduled the actual DPT session.

DPT was administered intramuscularly in the form of an aqueous solution containing 15 mg of substance per cm^3. The sessions were carried out in a special treatment suite, furnished like a comfortable living room with sofa, easy chairs, rugs, drapes, pictures, flowers and high fidelity stereophonic music equipment. The patient's therapist and a psychiatric nurse were in constant attendance throughout the period of drug action (4–6 h). For most of the session, the patient reclined on the sofa with eyeshades and stereophonic earphones alternately listening to carefully selected classical music or interacting with the therapist and nurse. One of the major goals of the therapist during the preparation period and the DPT session itself was to facilitate the occurrence of a psychedelic peak experience and help the patient to stabilize on this level. The therapeutic design of the DPT study allowed for repeated drug sessions if they were considered necessary or useful; the decision depended on the therapist's judgment based on previous clinical experience.

Following the DPT session(s), several additional drug-free interviews were required to work through, integrate and consolidate the events of the session(s). After completion of the course of psychedelic therapy with DPT and posttreatment testing, final disposition and discharge of the patient became the responsibility of the psychiatrist in charge of the ARU. After discharge from the hospital, no psychotherapeutic interviews were scheduled, and the patients were contacted only for the follow-up interviews and rating at the indicated intervals by the members of a separate evaluation team.

The group averaged 36.4 h of therapy, including the preparation and the drug session(s); the length of time in treatment from first to last therapy appointment was 2–22 weeks with an average of 8 weeks. The number of DPT administrations ranged between 1 and 6, with an average of 1.86 sessions.

Assessment of the Results

Pretreatment assessment. Before final acceptance into the experimental treatment program, the patients were given the following psychological tests: (1) Minnesota multiphasic personality inventory (MMPI), (2) Personality orientation inventory (POI), (3) Psychiatric evaluation profile (PEP), (4) Raven Progressive matrices, and (5) Benton visual retention test.

This pretreatment battery of psychological tests, besides providing a final

screening check for determining psychotic or organic brain impairment, served as a source of base line psychometric data against which posttreatment changes could be compared and evaluated.

In addition, each patient was seen by the social worker who discussed with him his past history and evaluated it with the use of a systematic social history questionnaire. This questionnaire, precoded for computer analysis, provides quantitative ratings on the patient's prehospital status during the 2 years preceding hospitalization. Its six 10-point rating scales allow for the quantification of the patient's status in the following areas: interpersonal, occupational, residential, and global adjustment; extent of alcohol consumption; and the degree of interference of the patient's drinking with his life adjustment. Repeat administrations of relevant sections of the social history questionnaire formed the basis for assessing the nature and course of treatment effects throughout the follow-up period. In some of the earlier patients of this series, an incomplete battery was administered; in addition, 3 patients were discharged from the hospital before the posttesting could be done.

Two samples of blood were drawn from the patients before the DPT session for the assessment of structural abnormalities of the chromosomes in the white blood cells; the results provided a base line for the assessment of the influence of DPT on the chromosomes. The analyses were done by Dr. *J.H. Tjio* at NIH in Bethesda, Md.

Assessment of the DPT sessions. The evaluation of the drug session was based on the observations and ratings of the therapist, on the subjective account written by the patient, and on the completion by the patient of a psychedelic experience questionnaire.

Posttreatment assessment. Between 3 and 5 days after the completion of treatment as described, the initial assessment battery of psychological tests was readministered. Two additional samples of blood were collected from each patient for the postsession chromosome analyses.

Follow-up assessment. The follow-up evaluations were carried out by social workers operating entirely independently of the clinical staff administering psychedelic therapy. The contact between the patient and the follow-up team was first made during the initial assessment period and then just prior to the patient's discharge from the hospital. Six months later, the status of the patient was reevaluated by the members of the follow-up team using the social history questionnaire, the same instrument that was used for the initial evaluation.

Data Analysis

All data were tabulated, punched on IBM cards and analyzed by a com-

puter. The effectiveness of the DPT treatment program was assessed by performing statistical tests of significance (direct difference t-tests) on the pre- and postpsychological test data and the pretreatment and follow-up ratings by social workers.

Results

Clinical Effects of DPT

Before initiating the present study, we experimented with various dosages and modes of administration to become acquainted with the basic clinical effects of DPT. The drug proved ineffective when ingested orally, and parenteral administration had to be used in all the experiments. The threshold dose for the induction of psychological changes appeared to be in the range between 10 and 15 mg. The highest dose employed in our clinical experimentation was 150 mg intramuscularly. The onset of the DPT reaction was usually between 5 and 20 min. The duration of the session showed a definite dependence on the dosage in addition to considerable interindividual variability. The duration of the low-dose DPT sessions (15–30 mg) was typically between 1.5 and 2 h, that of the high-dose sessions (60–150 mg) between 4 and 6 h. The termination of the DPT sessions was rather abrupt; we have not observed the prolonged fluctuations between the usual and the altered states of consciousness that are so characteristic of the LSD experience.

All 51 patients included in the present study received high doses of DPT (60–150 mg) after a special psychological preparation as described above. Administration of DPT produced very profound and dramatic experiences in almost all the patients. The phenomena observed in these sessions were very similar to the phenomenology of LSD sessions. They covered a very wide range from simple aesthetic experiences, through the reliving of emotionally relevant positive or negative memories with abreaction and catharsis, to profound psychedelic peak experiences of a religious or mystical nature.

The only striking differences between the effects of DPT and LSD that have important consequences for their clinical use were the necessity of parenteral administration of DPT, its rapid onset of action, the short duration of the DPT sessions and their abrupt termination.

Pre- to Posttreatment differences

Psychological test variables. Comparison of the pre- and posttreatment results from psychological testing indicated significant improvement in most of the measured parameters. Figure 1 shows the pre- and posttreatment composite profiles on the MMPI for 48 DPT patients. (For technical reasons the posttest data could not be obtained from three patients of the sample.) The immediate im-

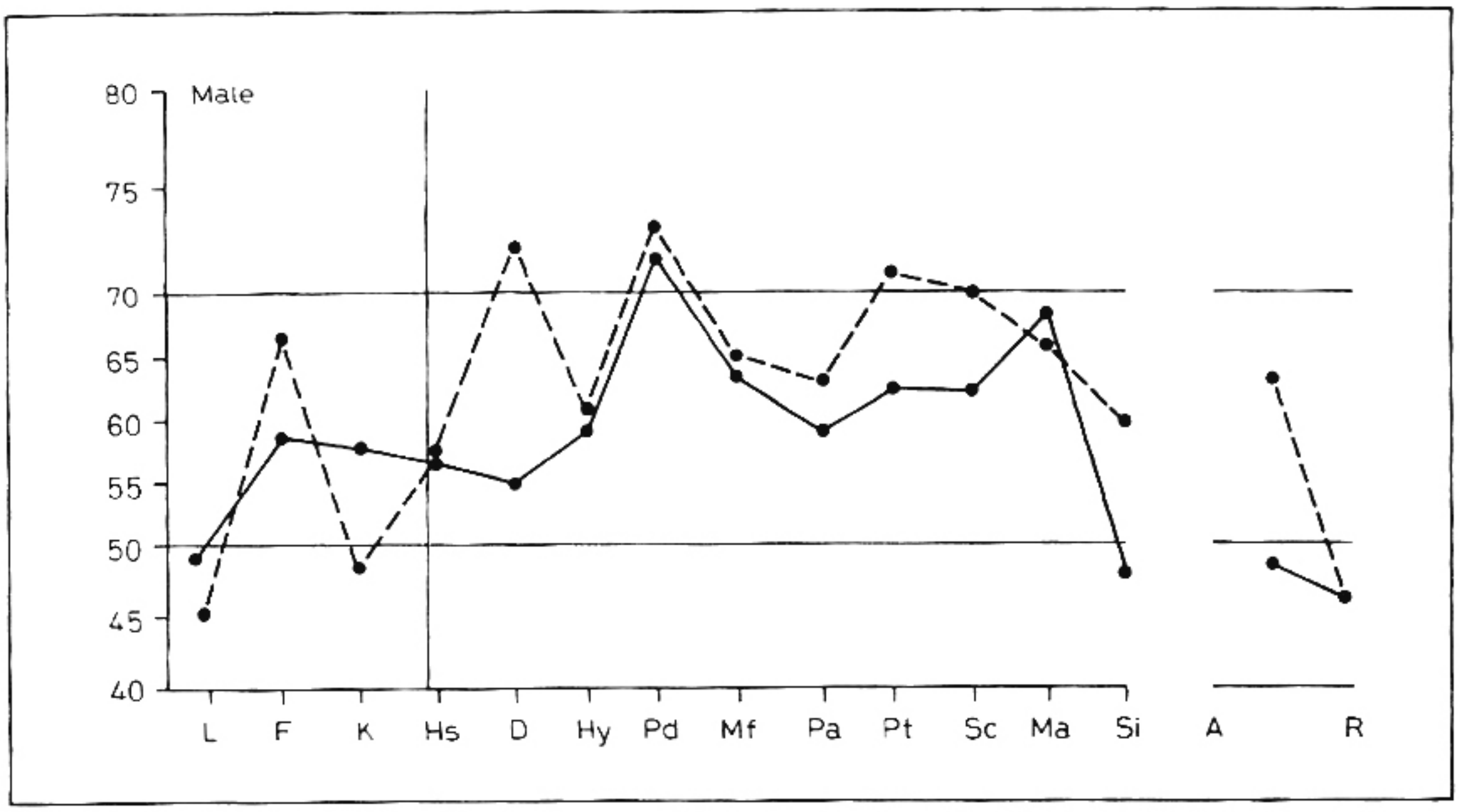

Fig. 1. Composite pre- (———) and posttreatment (——) MMPI profiles for 48 high-dose DPT patients.

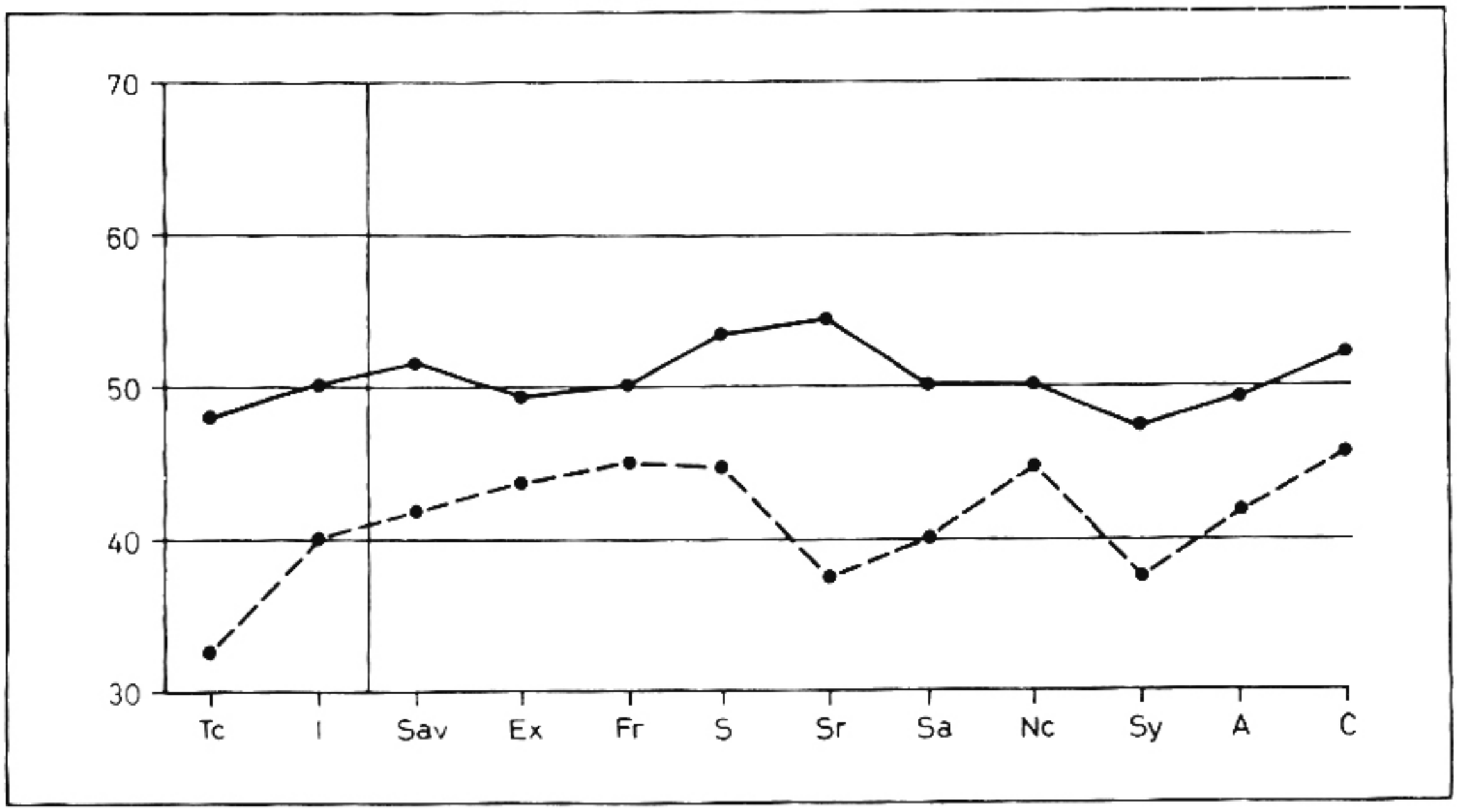

Fig. 2. Composite pre- (———) and posttreatment (——) POI profiles for 48 high-dose DPT patients.

provement following the DPT sessions was most significant in the categories of depression (D), Welsh's first factor (A), social introversion (Si), psychasthenia (Pt) and the F scale; for all these parameters, the change from pre- to posttesting was significant at the 0.001 level. The only scale showing a comparable significant increment following treatment was the K scale.

Figure 2 shows the pre- and post-composite profiles of the POI for these

48 patients. Comparison of these two curves indicates a significant improvement in all the scales of this test. All the increments are statistically significant at the 0.001 level. The most dramatic changes were observed in the scales of self-regard (Sr), time competence (Tc), inner-directed (I), the 0-I (support) ratio, self-actualizing value (SAV), and spontaneity (S). Pre- and posttreatment results of the Raven test were obtained from 47 DPT patients. The mean increment of the IQ was 4.39 points; this difference was significant at the 0.001 level. The pre- and postdata of the PEP test were compared in 36 patients. A significant improvement was observed in the scales of insight ($p < 0.001$), distress ($p < 0.001$) and SD ($p < 0.01$). The results in the remaining scales of this test were not significant. The Benton visual retention test administered to 44 of the high-dose DPT patients did not show significant differences from pre- to posttreatment.

Follow-up. From the total of 51 patients included in the study, 47 (92.1 %) could be located for follow-up assessment. Table II shows the pre- and posttreatment ratings of 47 patients in the dimensions of occupational, residential, interpersonal and global adjustment and abstinence. As the table indicates, a rather dramatic improvement can be seen in all the measured parameters of the social history questionnaire; the improvement in the abstinence, global adjustment and interpersonal adjustment scales are highly statistically significant ($p < 0.001$).

The percentage of patients functioning in an 'essentially rehabilitated' fashion is shown in table III. The criterion for acceptance of the patient into this

Table II. Differences of mean scores on the social history questionnaire from pretreatment to 6-month follow-up in 47 high-dose DPT patients

	Treatment	Follow-up	Mean difference	t	p
Occupational adjustment	4.89	6.62	+ 1.73	3.05	0.01
Residential adjustment	5.23	6.30	+ 1.07	2.66	0.02
Interpersonal adjustment	4.70	6.19	+ 1.49	4.14	0.001
Abstinence	3.36	7.17	+ 3.81	8.02	0.001
Global adjustment	4.00	6.68	+ 2.68	6.55	0.001

Table III. Percentage of alcoholic patients 'essentially rehabilitated' after high-dose DPT treatment (at 6-month follow-up)

Global adjustment	46.8 % (22/47)
Abstinence	53.2 % (25/47)

Score of 8, 9, or 10 on 0–10-point scale of the social history questionnaire.

category is a rating of 8 or more on the 0–10 scale of global adjustment and/or drinking behavior. In regard to global adjustment, this indicated that a patient was making 'good adjustment' with regard to drinking, occupation, interpersonal relations, etc. In regard to drinking behavior, a score of 8 indicated some, but only minimal, departure from total abstinence. From a group of 47 DPT patients, 22 (46.8 %) obtained this high score on the scale of global adjustment, and 25 (53.2 %) on the scale of abstinence. An even more impressive finding was that 18 patients (38.2 %) from the high-dose DPT group were totally abstinent at the 6-month follow-up (score of 10).

Discussion

The results of this exploratory clinical study seem to indicate that DPT can be used as an adjunct to brief intensive psychotherapy in alcoholic patients in a way comparable to LSD. According to our clinical and research experience, DPT can be administered with a reasonable degree of safety from the biological as well as psychiatric point of view.

A brief psychotic episode that occurred in one of the DPT patients 3 weeks after the last administration of the drug required readmission, but subsided rather quickly during conventional treatment with a tranquillizer (Mellaril). Although this episode started shortly after the last DPT exposure and appeared to be related to DPT sessions, it has to be taken into consideration that the patient had severe neurotic problems and symptoms before the sessions and that several rather powerful factors seemed to have contributed to it (prolonged drastic fasting, sleep deprivation and dehydration due to elimination of salt from diet).

The data from the chromosomal study are currently being processed; the preliminary findings do not suggest that DPT causes chromosomal damage in the white blood cells.

A comparison of the results of the DPT study with those of the LSD study mentioned previously shows that the degree of clinical improvement observed in the DPT group is very similar to that in the LSD group. Also, the results of the 6-month follow-up are comparable to the results for the high-dose LSD group. A direct, more accurate comparison of the DPT and LSD study cannot be made for several reasons. The groups of patients in both studies were not taken from the same pool by random assignment. They were taken from patient populations that were treated at a different time and by different therapists. The duration of the DPT sessions was considerably shorter, but more sessions were given on the average. The main significance of the pilot study with DPT was the clinical experience obtained with this new substance and some indication of its safety and usefulness in the treatment of alcoholism.

The major disadvantage of this study was the fact that, being a pilot study,

it did not have a concomitant control group; its results, rather impressive for a difficult group of alcoholic patients, cannot thus be compared with a sample of randomly selected patients from the same pool untreated or treated by an alternative method. Similarly, more conclusive quantitative comparison of the results with those of LSD-assisted psychotherapy will have to be made on the basis of a specially designed controlled study which is now in progress.

Acknowledgements

Appreciation is expressed to Dr. *Ferdinand Massari,* Director of the Alcoholic Rehabilitation Unit of Spring Grove State Hospital, for patient-referral and administrative cooperation; to Dr. *Thomas Hanlon,* Chief of Socio-Environmental Research at the Maryland Psychiatric Research Center, for statistical analyses; and to Dr. *Joe-Hin Tjio,* of the National Institute of Arthritis and Metabolic Disease, National Institute of Health, for chromosomal analyses of blood samples.

References

1 *Abramson, H.* (ed.): The use of LSD in psychotherapy and alcoholism (Bobbs-Merrill, New York 1967).
2 *Chwelos, N.; Blewett, D.B.; Smith, C.M., and Hoffer, A.:* Use of LSD-25 in the treatment of chronic alcoholism. Quart. J. Stud. Alcohol. *20:* 577 (1959).
3 *Faillace, L.A.; Vourlekis, A., and Szara, S.:* N,N-dipropyltryptamine, a new psychodysleptic drug. Proc. 5th Coll. Int. Neuro-Psychopharm., Washington 1966.
4 *Faillace, L.A.; Vourlekis, A., and Szara, S.:* Clinical evaluation of some hallucinogenic tryptamine derivatives. J. nerv. ment. Dis. *145:* 306 (1967).
5 *Hollister, L.E.; Shelton, T., and Drieger, G.:* A controlled comparison of lysergic acid diethylamide (LSD) and dextroamphetamine in alcoholics. Amer. J. Psychiat. *125:* 58 (1969).
6 *Kurland, A.; Savage, C.; Pahnke, W.N.; Grof, S., and Olsson, J.E.:* LSD in the treatment of alcoholics. Pharmakopsychiat. Neuro-Psychopharm. *4:* 83 (1971).
7 *Levine, J. and Ludwig, A.:* The hypnodelic treatment technique; in *Abramson* The use of LSD in psychotherapy and alcoholism (Bobbs-Merrill, New York 1967).
8 *Ludwig, A.; Levine, J.; Stark, L., and Lazar, R.:* The clinical study of LSD treatment in alcoholism. Amer. J. Psychiat. *126:* 59 (1969).
9 *MacLean, J.R.; MacDonald, D.C.; Byrne, U.P., and Hubbard, A.M.:* The use of LSD-25 in the treatment of alcoholism and other psychiatric problems. Quart. J. Stud. Alcohol. *22:* 34 (1961).
10 *Pahnke, W.N.; Kurland, A.A.; Unger, S.; Savage, C., and Grof, S.:* The experimental use of psychedelic (LSD) psychotherapy. J. amer. med. Ass. *212:* 1856 (1970).
11 *Smith, C.M.:* A new adjunct to the treatment of alcoholism. The hallucinogenic drugs. Quart. J. Stud. Alcohol. *19:* 406 (1958).
12 *Szara, S.:* The comparison of the psychotic effects of tryptamine derivatives with effects of mescaline and LSD-25 in self-experiments; in *Garattini and Ghetti* Psychotropic drugs (Elsevier, Amsterdam 1957).

13 *Szara, S.:* Hallucinogenic effects and metabolism of tryptamine derivatives in man. Fed. Proc. *20:* 885 (1961).
14 *Szara, S.:* Background information on the pharmacological and clinical data of N,N-dialkyltryptamine derivatives (unpublished, 1965).
15 *Szara, S.; Rockland, L.; Rosenthal, D., and Handlon, J.:* Psychological effects and metabolism of N,N-dietyltryptamine in man. Arch. gen. Psychiat. *15:* 320 (1966).
16 *Szara, S.:* DMT (N,N-dimethyltryptamine) and homologues. Clinical and pharmacological considerations; in *Efron* Psychotomimetic drugs (Raven Press, New York 1970).
17 *Vourlekis, A.; Faillace, L., and Szara, S.:* Psychotherapy combined with psychodysleptic tryptamine derivatives. Proc. 5th Coll. Int. Neuro-Psychopharm., Washington 1966.