HILLSIDE HOSPITAL

FOR PSYCHIATRIC TREATMENT, TRAINING AND RESEARCH

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JOSEPH S. A. MILLER, M. D.
MEDICAL DIRECTOR

SIMON KWALWASSER, M. D.
ASSOC. MEDICAL DIR.

MAURICE BACHRACH
ADMINISTRATOR

June 27, 1955

Dear Dr. Fink:

This is to acknowledge, with thanks, the receipt of $100 for the Research Fund, from yourself and your Associates, Hyman Korin and Simon Kwalwasser.

I am sure that there is no need for us to tell you of the importance of our research program. The Directors are appreciative of the sentiment underlying your gift of this $100. to Hillside Hospital.

Very sincerely yours,

Maurice Bachrach

MB:hm

cc: Dr. Kwalwasser
Dr. Miller
Mr. Korin

June 30, 1955

Somatic Therapy Research Program 1955-57

From the Research Service of the Hillside Hospital

A. AIMS: It is the purpose of this study to investigate the mode of action of somatic therapies in mental illness. We plan to do this by the systematic investigation of physiological, behavioral and personality factors which may be involved.

B. BACKGROUND: Although many theories concerning the therapeutic mechanism of the somatic therapies have been advanced, they have been either empirically disproved, or, are so vague that their validity cannot be tested. More recently, the development of a more meaningful hypothesis, and new methods of study have provided the opportunity for a fruitful investigation. In 1952, Weinstein and Kahn (Amer. Journal Psychiatry 109: 22-26) suggested that the somatic therapies lead to improvement by creating a milieu of altered brain function in which mechanisms of denial could operate. Some support for this hypothesis has been found in the literature. Carter (Am. Psychologist 8: 330, 1953) has confirmed some of the earlier work of Janis, showing that there is selective forgetting of unpleasant life memories after electroshock. Using tachistoscopic presentation of emotional and non-emotional words, Teicher (Am. Psychologist 8: 445, 1953) demonstrated that "mechanisms of repression" to emotional stimuli occur in the post-shock state.

For the past year and a half preliminary studies investigating this hypothesis have been done at these laboratories at Hillside Hospital. The results to date have been striking. Twenty-four consecutive electroshock patients were followed with serial electroencephalograms and amytal, simultaneous tactile perceptual and memory tests. A marked correlation between

improvement and early, persistant and severe changes on the electroencephalogram, and in the amytal tests was observed. If such changes did not appear, improvement did not occur. It is our conclusion that early and persistant changes in these indices are a necessary, though not sufficient, prerequisite for improvement. These observations make it possible to predict the short term response to therapy during the second and third week of treatment.

A report on the amytal test results was presented at the recent meeting of the American Psychiatric Association (May 1955) and submitted for publication to the American Journal of Psychiatry. At a meeting of the Electroshock Research Association on May 8th, a report of the changes in memory and learning occurring during the course of electroshock treatment was presented. This report was awarded the Annual Prize Award of the Association. The citation noted the methodology as exemplary, and offering a fruitful method of studying electroshock.

Concomitant with these studies, we have followed patients on insulin coma therapy. Recent reports on the value of prolonged coma as the basis for improvement (Kwalwasser and Caplan: J. Hillside Hospital 1: 145, 1952; Revitch, E. : Psychiat. Quart. 28: 72, 1954; Shagass and Rowsell: A.M.A. Arch Neurol. and Psychiat. 72: 705, 1954; and Yeager et al: J. Nerv. & Ment. Dis. 118: 435, 1954) have been confirmed in our patients in studies over the past 2 years. In one unusual case report the direct relationship between altered brain function, denial and improvement has been demonstrated (Delusional Reduplication of Parts of the Body After Insulin Coma Therapy, J. Hillside Hospital, 1955, in press).

C. METHOD: 1. We plan to verify and amplify our preliminary observations on the relation of changes in behavior to altered brain function after somatic treatment.

(a) Patients on electroshock will be given amytal tests (Weinstein, E.A. and Kahn, R.: Diagnostic Use of Amobarbital Sodium In Organic Brain Disease, Am. J. Psychiat. 109: 889-894, 1953; Serial Administration of the "Amytal Test" for Brain Disease: Its Diagnostic and Prognostic Value, A.M.A. Arch Neurol. and Psychiat. 71: 217-226, 1954) and electroencephalograms before and at stated intervals during treatment. This data will be used to make a prediction of the short term response to treatment.

(b) Double simultaneous tactile perceptual tests will be carried out using threshold electrical stimulation. Using two Grass S4-B stimulators, monitored by an oscillograph, the patient will be tested for his ability to perceive two stimuli applied simultaneously to different parts of his body. The technique of double simultaneous stimulation has been shown previously to be a good index of altered brain function (Fink et al, Neurology, 2: 46-58, January, 1952). By applying this highly refined technique it is hoped that changes in brain function which are not otherwise apparent will be elicited. As in the case of electroencephalogram and amytal tests, patients will be tested before and at stated intervals during treatment.

2. Other Physiological procedures will be carried out in conjunction with the tests above.

(a) Each patient will be given the mecholyl-epinephrine test as described by Funkenstein and associates (J. Nerv. Ment. Dis. 108: 409, Nov. 1948). The results will be compared with the work of previous investigators as well as with the results of our other physiological tests.

(b) Biochemical testing of patients undergoing electroshock and insulin coma treatment have been in progress for some time in these laboratories. In this series of patients, estimates of urinary ketosteroid excretion rates will be compared to their post-treatment excretion rate. Simultaneously estimates of steroid sulphates; phosphatase; and blood levels of steroid sulphate,

phosphorus, phosphatase and total alkaloid will be done.

3. It has been evident in our preliminary investigation that many of the patients that improve after somatic treatment relapse within six months. The critical problem of the factors involved in regard to the duration of improvement is also to be studied. One hypothesis now under investigation is that sustained improvement may be related to the premorbid personality. Specifically, patients with the characteristics of the "explicit verbal denial" personality (Weinstein, E.A. and Kahn, R.L.: Personality Factors in Denial of Illness, A.M.A. Arch. Neurol. & Psychiat. 69: 1-13, March, 1953) will be more likely to maintain improvement, than patients who do not have this premorbid personality makeup.

(a) Evaluation of the premorbid personality by interviews with at least two close relatives will be made for each patient. A standardized questionairre will be used to elicit characterological factors, which may have predictive value such as need to be right, prestige-consciousness, sensitivity to criticismand compulsive drive.

(b) Tachistoscopic presentation of pictures and words: The threshold levels of subject matter related to illness will be compared with material of more indifferent nature. This data will be evaluated for characterological indications. In addition, alterations in response will be assessed as quantitative indices of denial.

(c) The Thematic Apperception Test and the Rorschach will be given and evaluated for the same factors as the personality interviews.

(d) On the basis of the personality material, predictions of response to treatment will be made at different periods. Prior to the start of treatment patients will be classified according to three possibilities: 1) those unlikely to improve; 2) those likely to improve moderately or temporarily; and 3) those likely to maintain marked and sustained improvement (for at least 6

months). Prediction will also be made during the course of treatment (the third weekfor the electroshock patients) taking into account the physiological indices as well as the analysis of premorbid personality factors. At the conclusion of treatment patients will be evaluated for actual immediate response to the treatment. Those who showed some improvement will then be classified again according to whether or not improvement will be sustained.

4. Evaluation of the change in behavior of patients undergoing treatment will be made on the basis of a modification of the Malamud rating scales. Such ratings will be made independently of all the other test results by a supervising psychiatrist.

D. FACILITIES AVAILABLE: 1. Hillside Hospital is a 200 bed voluntary hospital for psychiatric care. All patients subjected to physiological therapies are available for study. Periods of hospitalization are 2-8 months; and a 4-6 week observation period is generally available prior to the institution of physical therapy.

A Research Service has been established, with a full time professional staff of a Director (neuropsychiatrist); assistant in psychiatry; biochemist and assistant chemist; research neurophysiologist (Ph.D.) and EEG technician and secretary. A full time psychologist and two chemists are associated on a project basis.

Laboratory facilities include: (a) Electroencephalographic unit with a Medcraft D-8, 8 channel instrument; (b) Neurophysiological laboratory with two S-4B Grass stimulators, Du Mont # 340 R oscillograph; two synchronized tachistoscopic projectors and auxiliary electronic equipment; (c) Biochemical laboratory with 1000 square feet of laboratory space and equipped with the following major items: Beckman spectrophotometer, Warburg respirator, Coleman Spectrophotometer, and radioisotope unit following the basic specifications of the A.E.C.

2. Personnel:

(a) Dr. Max Fink, M.D., Director of Research: After undergraduate studies at the University College of New York University where he received his B.A. cum laude with Honors in Biology in 1942, he attended the New York University College of Medicine, graduating in 1945. After a rotating internship he served in the U.S. Army, where he attended the School of Military Neuropsychiatry.

Formal neurologic training was received at Montefiore Hospital in New York (1948-1949) and at Bellevue Hospital (1949-1951). Formal psychiatric training received at Bellevue Psychiatric Hospital (6 months 1950) and then at Hillside Hospital (1952).

During 1951, and again in 1953, he was a research fellow of the National Foundation for Infantile Paralysis, first at New York University College of Medicine and then at Mount Sinai Hospital in New York. Both periods of study were under the supervision of Dr. Morris B. Bender.

In 1952 he was certified in Neurology by the Amer. Board of Psychiatry and Neurology, and was granted complementary certification in Psychiatry in May 1954. Simultaneously he attended and graduated from the William Alanson White Institute of Psychoanalysis, Psychiatry and Psychology, receiving their Certificate for Physicians in January 1953.

(b) Dr. Joseph Jaffe, M.D., Assistant in Psychiatry: Following undergraduate studies at Columbia College (B.A., 1944), Dr. Jaffe attended the New York University College of Medicine, and was granted his M.D. in 1947. He was elected to Alpha Omega Alpha. He was an interne at the Morrisania City Hospital, and then began three years intensive study at the Bellevue Psychiatric Hospital. First as a resident in psychiatry, then in neurology, and he completed his studies as a U.S.P.H.S. post-doctoral research fellow under the supervision of Dr. Morris B. Bender.

From 1951 to 1953 he was in the United States Air Force. He graduated from the School of Aviation Medicine and was Chief Psychiatrist at the Mitchell Air Force Base Hospital.

Since discharge from the military service he has been in the private practice of psychiatry. He was certified in psychiatry by the American Board of Psychiatry and Neurology in 1953. Since 1949 he has been a candidate in psychoanalysis at the William Alanson White Institute of Psychoanalysis, Psychiatry and Psychology; and for the past two years Research Assistant in Neurology at the Mount Sinai Hospital of New York.

(c) Dr. Robert L. Kahn, Ph.D.: Assistant in Neurophysiology: After graduation from Brooklyn College in 1940, he started graduate work at Columbia University which was interrupted by four years of service in the United States Army. In the army he went to Clinical Psychology School and served as psychologist in various hospitals within this country and overseas. On leaving the army he became a Research Psychologist in the Department of Neurology of the Mount Sinai Hospital in New York, where he has worked under the supervision of Dr. M. B. Bender and Dr. E. A. Weinstein up to the present time. To date, he has been an author of more than twenty publications, and is co-author of the monograph. "Denial of Illness: Symbolic and Physiological Aspects" which was published in May, 1955.

He received his Ph. D. from the New York University School of Graduate Arts and Sciences in 1953, and was an instructor of psychology at Brooklyn and Hunter Colleges for two years. For the past two years he has been a consultant to the New York State Department of Mental Hygiene and has conducted training programs in several of the mental hospitals.

(d) Dr. Harry Goldenberg, Ph.D.: Director of Laboratories and Chief Chemist: A graduate of C.C.N.Y. in 1944, where he was a recipient of the Tremaine Scholarship and graduated cum laude, Dr. Goldenberg received his Ph.D. in

1949 from the Polytechnic Institute of Brooklyn. He has been an instructor in biochemistry at the Polytechnic Institute (1946-47) and at Brooklyn College (1951 to date). In 1947-49 he was a Research Fellow in enzymology of the National Institute of Health, and from 1950 to 1952 he was a chemist to a U.S.P.H.S. project at Jewish Hospital of Brooklyn studying enzyme methods in clinical chemistry.

(e) Mr. Hyman Korin, Research Assistant (Psychology): Following four years of military service, he matriculated at College of the City of New York and received his B.S. in 1949 and his M.S. in 1950. During 1951-52 he was psychology interne at the Mount Sinai Hospital and matriculated for his Ph.D. at New York University. Since June 1953 he has been Research Assistant in Psychology at Hillside Hospital and has recently completed his doctoral thesis on "The Effects of Electroshock on Retroactive Inhibation."

3. Publications: Recent publications of the Research Service include:

The Amytal Test in Patients with Mental Illness, J. Hillside Hospital, 4: 3-13, 1955.

Relation of Changes in Memory and Learning to Improvement in Electroshock, Conf. Neurologica, 1955 (In press).

Delusional reduplication of Parts of the Body After Insulin Coma Therapy, J. Hillside Hospital, 1955 (In press).

Relation Between Altered Brain Function and Denial in Electroshock Therapy, Amer. J. Psychiatry (submitted).

Rectification of Nonlinear Beer's Law Plots, Anal. Chem. 26: 690, 1954.

Rectification on Non-Linear Enzyme Activity Curves, Arch Biochem. and Biophys., 52: 288, 1954.

July 1, 1955

BUDGET - RESEARCH SERVICE, 1955-56

		USPHS	BD OF DIRECTORS
1. PERSONNEL			
Director of Research	15,000	-	15,000
Research Assistant in Psychiatry	7,200	-	7,200
Research Assistant in Neurophys.	7,500	7,500	-
Chief Chemist	8,200	-	8,200
Assistant Chemist	2,800	-	2,800
Research Assistant in Psychology	4,000	4,000	-
Assistant Chemist	4,000	4,000	-
Assistant Chemist	1,800	1,800	-
Secretary - EEG Technician	2,520	960	1,560
2. EQUIPMENT	150	150	
3. CONSUMABLE SUPPLIES	3,810	2,140	1,670
4. TRAVEL-CONFERENCES	1,000	200	800
TOTAL	$ 57,980	$20,750	$37,230

July 8, 1955

MEMORANDUM

TO: Dr. Joseph S. A. Miller

FROM: Dr. Max Fink

SUBJECT: Monthly Report - Research Service - June

1. Members of the Research Service continued the various projects of the service, and prepared a number of protocols for presentation to various foundations for support. The protocol of the project with the Sloan-Kettering Institute was completed, approved by the Medical Director, and submitted to the Research Committee on June 29th. The approval of the Research Committee was obtained, and the project was begun under the direction of Dr. H. Goldenberg and Dr. J. Royce.

Supplementary grant M-927 of the U.S. Public Health Service was approved, effective September 1st, 1955.

2. PAPERS PRESENTED: None. The book, "Denial of Illness", by Dr. Edwin A. Weinstein and Robert L. Kahn was published during this month.

3. MEETINGS ATTENDED: The Annual Meeting of the American Psychopathological Association was attended in New York City. The subject was, "experimental Methods in Psychiatry", and much valuable material was presented.

4. ONGOING PROJECTS:

A. Electroshock #2: A collection of data for this project is continuing. Preliminary estimates show that the original speculation on the relation between character and outcome of electroshock treatment will probably be borne out by the data.

B. Ambivalence: Doctor Tarachow has continued to come out for this project and further data has been collected. A review of the work of the past four or five months has shown that some correlations, specifically the TAT and the clinical interview, were excellent. There will be further continuation of this project after the summer recess.

C. Serpasil: Studies have continued and a fairly clear picture of the role of serpasil in behavior has been developed. It should be possible by the end of the summer to write a definitive report.

D. Subculture: The work of this committee has been hampered by Dr. R. Navarre's other duties, but they have held a number of meetings and anticipate beginning with a single patient as a pilot project. This should be begun in the first week in July.

E. Sloan-Kettering Project: Two patients have been selected and the initial urine samples have been collected. One patient is now on serpasil, and the second patient is under electroshock treatment. It is anticipated that repeat collection of samples will be made after therapy is ended.

5. NEW PROJECTS: None.

6. FUNDS: The second year grant for the biochemical and neurophysiological grants were both approved. A supplementary grant request for $7992.00 was approved by the Public Health Service for the M-927 project. This money will cover the salary of Dr. R. Kahn.

In addition, protocols were submitted through Mr. Coleman to the Hofheimer Foundation.

Department of Biochemistry ..... Dr. H. Goldenberg

RESEARCH PROGRESS REPORT, JULY-AUGUST 1955

A. Major Work in Progress

1. Determination of Chlorpromazine in Blood and Urine

The procedure for the colorimetric estimation of chlorpromazine and related alkaloids, described in the June 1955 progress report, has been further refined to permit detection of the extremely small amounts of drug circulating in blood. The method is based on two new features: (1) The finding that drugs can be quantitatively extracted from biological fluids with a single portion of an ethylene dichloride-ether solvent mixture, and (2) The use of a three-phase solvent dye partition system of analysis.

Clinical data are also being obtained on bound as well as free circulating promazine, based on the use of hot acid to liberate the conjugated drug.

2. Inhibition of Cholinesterase by Hallucinogens

These studies are being continued as indicated in the prior report.

3. Steroid Sulfate Conjugates

All but one of the major problems involved in the assay of steroid sulfate metabolism in mental disease have now been solved. A novel device has been introduced for eliminating the interference with our test due to phenol sulfates in blood and urine. A two-phase system incorporating dicyclohexylamine (DCHA) as a complexing agent effectively separates the steroid from the phenol sulfates, permitting their unequivocal determination. The procedure for serum is now as follows:

a. Serum is treated with alkali to release the hormone conjugates.
b. A lipid solvent is added to precipitate the proteins and simultaneously extract the hormones.
c. The lipid supernate is brought to dryness and partitioned between DCHA and chloroform.
d. The free steroid sulfates are released by shaking the chloroform extracts with acidic resin.
e. Final assay of the sulfate conjugates is effected by adding dye and reading the color.

A considerable amount of clinical data have already been obtained on normal people and on patients selected for independent studies by the Sloan-Kettering Institute. An immediate correlation has been established in our laboratory between urinary conjugate levels and sex, males excreting about twice as much conjugate as females. This ties in well with what is known of steroid metabolism

and tends to confirm the validity of the method.

Attention is now being devoted to fractionation of the steroid hormones in conjugate form. Paper electrophoresis has proven inadequate for the purpose. Paper chromatography is more successful and is under continuing study.

B. Papers, Lectures and Conferences

The following papers are in preparation: (1) "Colorimetric Determination of Alkaloids, with Particular Reference to Chlorpromazine", and (2) "Steroid Sulfate Conjugates. II. Colorimetric Microestimation".

C. Funds and Personnel Changes

1. Research Grant #A-675 from the National Institutes of Health was renewed for the fiscal period Sept. 1955 - Aug. 1956.

2. Messrs. Michael Miller and Spencer Parness terminated their summer employment in the laboratory at the end of August.

cc. to: Dr. Fink
Dr. Miller

Department of Biochemistry ..... Dr. H. Goldenberg

RESEARCH PROGRESS REPORT, SEPTEMBER 1955

A. Major Work in Progress

1. Determination of Chlorpromazine in Biological Fluids

As a result of repeated analyses of blood drawn from patients receiving chlorpromazine, the circulating blood level has been established as less than 1 microgram per ml. serum. The three-phase solvent dye partition scheme of analysis mentioned in the previous report has therefore been adopted as the only method capable of detecting the extremely minute amounts of drug in peripheral blood. A new shaking machine has just been obtained from the A.H. Thomas Co., Philadelphia, to permit application of the method on a broad scale.

The question naturally arises as to the metabolic fate of chlorpromazine in humans. We have recently detected in patients' urine an ether-soluble carboxylic acid which reacts with ferric chloride and appears to be an oxidative by-product of chlorpromazine metabolism.

2. Inhibition of Cholinesterase by Hallucinogens

The three-phase system mentioned above has been found applicable to the analysis of LSD 25 as well as chlorpromazine and serpasil. By combining this observation with the earlier discovery of the inhibitory effect of LSD 25 on human serum cholinesterase, it is now possible to relate the enzyme inhibitory action to the alkaloid concentration in "unknown" samples of fluid and so determine the specific molar inhibitory action at the 0.1 microgram level. This amounts, in effect, to the first sensitive chemical test ever reported for the detection of LSD 25 and related hallucinogens.

3. Steroid Sulfate Conjugates

Work progressing essentially as described in July-August report.

cc. to: Dr. M. Fink
Dr. Jos. S.A. Miller

File
J.S.M.

October 10, 1955

MEMORANDUM

TO: Dr. Joseph S. A. Miller

FROM: Dr. Max Fink

SUBJECT: Quartarly Report of the Research Service - July to September 30th, 1955

This quartarly period was marked by a variety of significant events in the Research Service. While the period is an extended one, it was interrupted by the summer hiatus. Five subjects are worthy of mention: 1.) The completion of electroshock number 2. 21) The augmentation of our staff by the appointment of Doctor Joseph Jaffe. 3.) The preparation of a protocol for the Ford Foundation, and the submission of minor protocols to other organizations. 4.) The beginning of a Thorazine-Insulin project. 5.) The establishment of satisfactory techniques for the isolation and determination of chlorpromazine, serpasil, and steroid sulphate compounds.

Following our summaries of the present status of various projects.

1.) <u>Ongoing projects:</u>

A.)Electroshock # 2: The final group of patients were tested during the month of July, and as of August 1st the project was terminated with a total number of patients of 27. This data is now being analyzed, and the results will be presented probably by the middle of November.

B.)Ambivalence: There has been considerable discussion about this project, which is going to go into full swing this month. Three aspects of the problem are going to be correlated; the clinical evaluation of ambivalence, the TAT evaluation, and the tachistoscopic. In July, Dr. Tarachow added a number of variations to this part of the project, specifically, drawings made by the subject following the rapid exposure of a simple

figure. Such drawings, made after a picture has been exposed for to short of a time to be clear, may reflect some of the patients basic problems.

C.) Serpasil: This project has continued, and will be completed at the end of this month. Seventeen patients have been studied, and of these two are still in the course of study at this time. Early correlations of the clinical observations and the laboratory studies show, that Serpasil, in the doses administered, is not an effective agent. Patients who were depressed, manifested an exaggeration of this symptom. Patients who were over-active, showed some alleviation of this activity, but the psychotic ideation and disturbed behavior generally continued. There was some minimal interference with anxiety symptoms, but this was replaced in general by many somatic symptoms. In the evaluation of the mecholyl responses following serpasil, there was a consistent affect in all subjects. The general blood pressure response was five to ten points lower in every subject. Doctor Blumberg feels that this data is of significance and some consideration is being given to present this at the next American Psychosomatic Society meeting.

D.) Subculture: This group has studied a single patient over the past few months and have collected considerable data which they are studying in anticipation of formulating a protocol. With the relief on October 1st of Dr. Navarre as part time supervisor in the Adolescent Pavilion, it is anticipated that this project will continue at a greater pace.

E.) Sloan-Kettering Project: Urine studies have been carried on during the past few months. Three collections were taken on a patient who was markedly disturbed prior to electroshock and who showed a significant response to this treatment. Two other patients have been started and a fourth patient, who had been started did not complete his studies as he left the hospital precipitously. I also had a number of meetings with Doctors Hellman and Gallagher and this project seems to be going along quite well.

At the suggestion of Dr. Hellman, three patients were given daily doses of dehydroisoandrostrone. All three patients were schizophrenics, and the observations were made by the therapist, Dr. Stanley Friedman. After four weeks of administration, there appeared to be no significant change in behavior, and there were no complications in the therapy. Dr. Goldenberg was able to obtain urine samples during this period for further studies to the elimination of this agent.

F.) Double Simultaneous Stimulation: During the past few months artefactshave been eliminated from the electrical stimulator. We have made some preliminary runs on patients both prior to and after electroshock, and it is apparent that there is a significant change in this perception with treatment. It is anticipated that the onset of the project Electroshock #3, that this part of the project will be instituted as of October 1st.

2.) <u>New Projects:</u>

A.) Language Changes Following Electroshock Therapy: On September 1st, Dr. Jaffe began work in our department and is active in developing a number of tests and approaches to the question of language and behavior changes following shock treatment. It is our anticipation that this work will be ready for electroshock #3.

B.) Thorazine-Insulin Coma Project: When it was apparent that insulin coma therapy was to be altered for an extended period of time because of the shortage of nurses, it was recommended that the drug Thorazine be tested as a substitute for insulin. Dr. Shaw, who had had some experience with Thorazine, approached me and this project was then undertaken. For the past month all patients who had been screened by the supervising psychiatrist for physical treatment, have fallen into three groups - those recommended for electroshock, those recommended for insulin, and those recommended for no physical treatment. All patients in the second group were then assigned

to the Insulin-Thorazine group. Seven such patients are now under investigation. Our preliminary results after three weeks work, demonstrate a marked clinical effect of thorazine when given in very large doses. Doses have run from 2,000 to 3,600 miligrams daily.

3.) Papers Presented:

A.) On September 30th the paper entitled "Quantitative Study of Slow Wave Activity Following Electroshock" was presented at the Combined meeting of the Eastern and Southern Electroencephalographic Societies, held at the National Institutes of Health, Bethesda on September 30th. There was considerable discussion and it appeared that this paper was well received.

B.) The Research Service has been invited by the Nassau Neuropsychiatric Society to present a summary of our observations on Thorazine and Serpasil at their November meeting.

4.) Meetings Attended:

1.) During the summer recess, I had the opportunity to meet with Dr. Norman Reider in San Francisco, and with Drs. Modlin and Wallerstein at Topeka. At both these meetings I took the opportunity to express our interest in increasing our staff in the line of a psychoanalitically oriented psychiatrist.

B.) Following the meetings of the Eastern Electroencephalographic Association, Drs. Kahn, Korin and myself visited the National Institute Clinical Center at Bethesda and toured the various laboratories. Some of our observations presented to the residents at the monthly research seminars.

C.) Nassau Neuropsychiatric Society: The September meeting of the Nassau Society presented a symposium on the relationship of the new New York State Mental Health Law and the various community services. Much

valuable information was obtained at that meeting, and some of the observations were discussed with Drs. Lennzner and Luttrell.

5.) Funds:

A.) In July, a protocol was submitted to the Kaufmann Foundation, for support of the project of Dr. Jaffe. This was done at the request of Mr. Coleman.

B.) During the past few months, we have devoted considerable time to developing a protocol satisfactory for the Ford Foundation. Our program entitled "An Evaluation of Psychiatric Therapies" was presented to the Research Committee in September. It was the consensus that the protocol was not satisfactory and numerous recommendations were made for correction. This will be done in the next few weeks.

C.) On September 17th, Dr. Jerome D. Frank, as a representative of the National Institute of Mental Health, interviewed us at Hillside with regard to our application to the USPHS.

6.) Other Activities:

A.) Israel Strauss Lecture: There has been considerable discussion among the members of the Israel Strauss Lecturship Committee and consideration is being given to Dr. Malamud as the next lecturer. Further discussion along this line is necessary, however.

B.) Israel Strauss Volume of the Hillside Journal: Following some initial discussion between Dr. Tarachow and myself, the memorial volume for Dr. Strauss was presented to the Medical Board and then to the Publications Committee. We have undertaken to carry out the screening and various office procedures necessary for this volume.

C.) Dr. Karliner's Project: Following our discussion in June, Dr. Karliner spent a number of weeks working out a new protocol. This was discussed at the end of September and it is hoped that the program can be implimented

during the next month.

D.) Ruder and Finn: This agency has made numerous overtures to the hospital regarding a film about creative therapy. This was discussed at the Research Committee meeting and since then a meeting has been planned between Mr. Finn and Dr. Miller to discuss the possibilities of a Research Study of creative therapy rather than a film.

Respectfully submitted,

Max Fink, M.D.

October 10, 1955

MEMORANDUM

TO: Dr. Joseph S. A. Miller

FROM: Dr. Max Fink

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C.) Serpasil: This project has continued, and will be completed at the end of this month. Seventeen patients have been studied, and of these two are still in the course of study at this time. Early correlations of the clinical observations and the laboratory studies show, that Serpasil, in the doses administered, is not an effective agent. Patients who were depressed, manifested an exaggeration of this symptom. Patients who were over-active, showed some Allaviation of this activity, but the psychotic ideation and disturbed behavior generally continued. There was some minimal interference with anxiety symptoms, but this was replaced in general by many somatic symptoms. In the evaluation of the mecholyl responses following serpasil, there was a consistent effect in all subjects. The general blood pressure response was five to ten points lower in every subject. Doctor Blumberg feels that this data is of significance and some consideration is being given to present this at the next American Psychosomatic Society meeting.

D.) Subculture: This group has studied a single patient over the past few months and has have collected considerable data which they are studying in anticipation of formulating a protocol. With the relief on October 1st of Dr. Navarre as part time supervisor in the Adolescent Pavilion, it is anticipated that this project will continue at a greater pace.

E.) Sloan-Kettering Project: Urine studies have been carried on during the past few months. Three collections were taken on a patient who was markedly disturbed prior to electroshock and who showed a significant response to this treatment. Two other patients have been started and a fourth patient, who had been started did not complete his studies as he left the hospital precipitously. I also had a number of meetings with Doctors Hellman and Gallagher and this project seems to be going along quite well.

At the suggestion of Dr. Hellman, three patients were given daily doses of dehydroisoandrostrone. All three patients were schizophrenics, and the observations were made by the therapist, Dr. Stanley Friedman. After four weeks of administration, there appeared to be no significant change in behavior, and there were no complications in the therapy. Dr. Goldenberg was able to obtain urine samples during this period for further studies to the elimination of this agent.

F.) Double Simultaneous Stimulation: During the past few months artefactshave been eliminated from the electrical stimulator. We have made some preliminary runs on patients both prior to and after electroshock, and it is apparent that there is a significant change in this perception with treatment. It is anticipated that the onset of the project Electroshock #3, that this part of the project will be instituted as of October 1st.

2.) <u>New Projects:</u>

A.) Language Changes Following Electroshock Therapy: On September 1st, Dr. Jaffe began work in our department and is active in developing a number of tests and approaches to the question of language and behavior changes following shock treatment. It is our anticipation that this work will be ready for electroshock #3.

B.) Thorazine-Insulin Coma Project: When it was apparent that insulin coma therapy was to be altered for an extended period of time because of the shortage of nurses, it was recommended that the drug Thorazine be tested as a substitute for insulin. Dr. Shaw, who had had some experience with Thorazine, approached me and this project was then undertaken. For the past month all patients who had been screened by the supervising psychiatrist for physical treatment, have fallen into three groups - those recommended for electroshock, those recommended for insulin, and those recommended for no physical treatment. All patients in the second group were then assigned

to the Insulin-Thorazine group. Seven such patients are now under investigation. Our preliminary results after three weeks work, demonstrate a marked clinical effect of thorazine when given in very large doses. Doses have run from 2,000 to 3,600 miligrams daily.

3.) Papers Presented:

A.) On September 30th the paper entitled "Quantitative Study of Slow Wave Activity Following Electroshock" was presented at the Combined meeting of the Eastern and Southern Electroencephalographic Societies, held at the National Institutes of Health, Bethesda on September 30th. There was considerable discussion and it appeared that this paper was well received.

B.) The Research Service has been invited by the Nassau Neuropsychiatric Society to present a summary of our observations on Thorazine and Serpasil at their November meeting.

4.) Meetings Attended:

A.) During the summer recess, I had the opportunity to meet with Dr. Norman Reider in San Francisco, and with Drs. Modlin and Wallerstein at Topeka. At both these meetings I took the opportunity to express our interest in increasing our staff in the line of a psychoanalitically oriented psychiatrist.

B.) Following the meetings of the Eastern Electroencephalographic Association, Drs. Kahn, Korin and myself visited the National Institute Clinical Center at Bethesda and toured the various laboratories. Some of our observations presented to the residents at the monthly research seminars.

C.) Nassau Neuropsychiatric Society: The September meeting of the Nassau Society presented a symposium on the relationship of the new New York State Mental Health Law and the various community services. Much

valuable information was obtained at that meeting, and some of the observations were discussed with Drs. Lennzner and Luttrell.

5.) Funds:

A.) In July, a protocol was submitted to the Kaufmann Foundation, for support of the project of Dr. Jaffe. This was done at the request of Mr. Coleman.

B.) During the past few months, we have devoted considerable time to developing a protocol satisfactory for the Ford Foundation. Our program entitled "An Evaluation of Psychiatric Therapies" was presented to the Research Committee in September. It was the consensus that the protocol was not satisfactory and numbrous recommendations were made for correction. This will be done in the next few weeks.

C.) On September 17th, Dr. Jerome D. Frank, as a representative of the National Institute of Mental Health, interviewed us at Hillside with regard to our application to the USPHS.

6.) Other Activities:

A.) Israel Strauss Lecture: There has been considerable discussion among the members of the Israel Strauss Lecturship Committee and consideration is being given to Dr. Malamud as the next lecturer. Further discussion along this line is necessary, however.

B.) Israel Strauss Volume of the Hillside Journal: Following some initial discussion between Dr. Tarachow and myself, the memorial volume for Dr. Strauss was presented to the Medical Board and then to the Publications Committee. We have undertaken to carry out the screening and various office procedures necessary for this volume.

C.) Dr. Karliner's Project: Following our discussion in June, Dr. Karliner spent a number of weeks working out a new protocol. This was discussed at the end of September and it is hoped that the program can be implimented

during the next month.

D.) Ruder and Finn: This agency has made numerous overtures to the hospital regarding a film about creative therapy. This was discussed at the Research Committee meeting and since then a meeting has been planned between Mr. Finn and Dr. Miller to discuss the possibilities of a Research Study of creative therapy rather than a film.

Respectfully submitted,

Max Fink, M.D.

October 20, 1955

MEMORANDUM

TO: Dr. Joseph S. A. Miller

FROM: Max Fink, M.D.

SUBJECT: Six Months Report of Research Activities at Hillside Hospital

At the request of the Chairman of the Medical Affairs Committee, I am submitting this six month report of the activities of the Research Service and associated research activities at the hospital. During this period, numerous projects have been under investigation, our staff has expanded, and our space requirements were met. Two projects are being completed, and one project has just been instituted.

A. PROGRESS IN ONGOING PROJECTS:

1. ELECTROSHOCK # 2: Our second electroshock project was undertaken in March 1955, and completed in September. Our first project had clearly demonstrated that cerebral changes were essential to improvement and that these could be measured by the electroencephalogram and by amytal tests. We also concluded that memory tests were a poor index of improvement and believed that there were specific psychological patterns indicative of denial which were more prominent in the improved group than in the unimproved. Following this study, the second project was undertaken and was designed to demonstrate the reliability of the electroencephalogram and the amytal tests for prognostic purposes; and to ascertain the characterological aspects which might be factors in the long term and short term results. We have studied twenty-seven patients to date. The data of this project is now being processed, and will be available following our six month follow up period, (which is from November to January).

The data from the first study was presented at various meetings, including the American Psychiatric Association, the Electroshock Research Association, and the Eastern Association of Electroencephalographers. The memory data, presented by Mr. Korin at the Electroshock Research Association in May, was awarded their annual prize.

The electroshock project # 3 is now in the planning stage (see below), and will be instituted November 15.

2. AMBIVALENCE: This project, which has been undertaken with Dr. Sidney Tarachow of the Medical Board, has accomplished a considerable amount of its basic work. Three approaches to the problem of measuring ambivalence have been accepted. These include an interview evaluation; the thematic apperception test, and tachistoscopic presentation of pictures. During this period of evaluating methods, twenty-three patients have been studied. Dr. Tarachow has been attending to this work, and the testing has been undertaken by Mr. Korin.

3. SERPASIL: The Serpasil evaluation study, undertaken at the end of last year, is completed. Seventeen patients have been studied intensively by a double blind technique. The data is now being evaluated by Drs. Blumberg and Wachspress. To date, the clinical results are disappointing. Patients who were depressed, manifested an exaggeration of this symptom. Patients who were over-active and disturbed/an alleviation of this activity but the psychotic ideation generally persisted. The intramuscular dosages induced a variety of secondary complaints. In the evaluation of the mecholyl responses following serpasil, there was a consistent effect in all subjects. The blood pressure response was significantly lower and Dr. Blumberg is considering presentation of this data at the next meeting of the American Psychosomatic Society.

showed

4. THORAZINE: Preliminary studies by Dr. Laderman in 20 patients in a series of clinical studies showed symptom and behavioral alterations but this was not significant in the doses used. In mid-September, Dr. Shaw undertook an evaluation of Thorazine as a possible substitute for insulin coma therapy. A protocol approved by The Research Committee, was submitted to Smith, Kline and French and approved, assuring us of adequate supplies for the duration of our project. In this study, patients will receive medication for a period of 8 to 12 weeks, comparable to the insulin coma period. During this time, very large doses of thorazine will be used. To date, eight patients have been studied. The dosages range from 1500 to 3600 mg. daily. The initial observations show that three patients had a significant clinical response; three patients had minimal changes; one patient developed toxic symptoms, and one patient has just begun the medication. Drs. Cohen and Blumberg of the medical department have contributed the necessary controls to permit our using such large doses of this potent drug.

5. SLOAN KETTERING STUDY: Since June, Drs. Goldenberg and Royce have been cooperating with the chemists at the Sloan-Kettering Institute in a study of the possible alteration in the keto-steroid excretion patterns in our patients. This study was approved by our Research Committee in June. Since then five patients have been under investigation. The initial data is not yet available. Each of the patients is being studied by Dr. Goldenberg in his laboratory as well as by the chemists at the Institute.

6. BIOCHEMICAL RESEARCH: Dr. Goldenberg has been occupied in studies measuring chlorpromazine, estimating the effects of lysergic acid and devising methods to measure steroid sulphate conjugates. This basic research is necessary to provide the methods of measurement which we plan to apply to our patients.

(a) Chlorpromazine: An ultra-sensitive technics has been developed which can measure minute (0.1 microgram) amounts of this drug. By applying this to a number of patients receiving Thorazine, Dr. Goldenberg has demonstrated that only very small amounts appear in the bloodstream.

(b) LSD: The inhibition of serum cholinesterase by LSD has been demonstrated, and this test applied to other hallucinogenic compounds. A correlation between hallucinogenic activity and cholestesterase inhibition was found.

(c) Steroid Sulphate Conjugates: With the grant support from the USPHS, methods to estimate these compounds have been devised. By studying liver slices, Dr. Goldenberg demonstrated that hormone sulphates are synthesized by the liver, and that there is a sex difference in the level of steroid excretion. Both these observations are of fundamental significance, and will be presented to various societies this winter.

7. MECHOLYL: In the Department of Medicine, Drs. Cohen and Blumberg have continued their Mecholyl studies of the electroshock and the serpasil patients. During this period an additional 40 patients have been studied and more than half have had more than one such evaluation. The serpasil group demonstrated a significant alteration in their blood pressure patterns following this drug. The electroshock data has yet not been correlated and will be done as soon as our electroshock # 2 data is available.

8. SUBCULTURE: Following the approval of this project by the Research Committee last spring, Drs. Navarre and Graubert had a number of meetings with members of the Medical Board. Following these discussions, they have begun a pilot study of one patient, and intend to evaluate those factors in the hospital environment which may be contributory to the patient's improvement. This pilot study was undertaken in an effort to clarify a protocol satisfactory to the Research Committee and of sufficient quality to be submitted for financial support to outside organizations. To some extent, this project was hampered by the multiple duties of members of the committee and by the resignation of Dr. Gurvitz. Since September, however, the committee has been working very actively and it is anticipated that a satisfactory protocol will be available by the end of the year.

9. DIVIDED INSULIN DOSES: In June, following some discussions concerning the correct doses of insulin for insulin coma treatment, Drs. Laderman and Blumberg undertook an investigation into the relation between multiple doses os insulin and the blood glucose level. It was anticipated that multiple small doses of insulin might reduce blood sugar significantly earlier and for longer periods than a single large dose. It was quickly determined, however, that multiple small doses, even if the sum total was equal to a single dose, did not produce coma of a satisfactory degree and depth. This project is now being prepared for publication.

B. PROJECTS PLANNED:

1. Electroshock # 3: Beginning November 1st, the third electroshock project will be undertaken. This study is designed to extend our experience with the factors which may be relevent in both the long and short term clinical responses following electroshock. Also, in this study specific emphasis is placed on the psychiatric and language changes which follow electroshock treatment and which we have been accustomed to calling "improvement." Dr. Joseph Jaffe has prepared a number of specific studies, including detailed interviews with patients prior to and during treatment, in which specific aspects of behavior and language will be assessed.

In this study, also, a basic problem in the perception of multiple simultaneous tactile stimuli will be undertaken. Under our original grant from the United States Public Health Service, we were given funds to study the problem of satisfactorily delivering single and multiple independent electrical square wave impulses. The equipment was designed and completed in September and for the past few weeks has been undergoing rigorous clinical tests. It has been found highly satisfactory and will be applied during this project with the specific question of the relation between changes in double simultaneous stimulation tests and changes in behavior, in the electroencephalogram and in amytal tests following electroshock.

2. BIOCHEMICAL APPLICATION OF NEW TESTS: Dr. Goldenberg has completed the pilot studies necessary to devise measures of specific compounds. He believes these should be applied to our clinical population over the next year. A specific protocol for this application is being prepared.

3. PROGNOSTIC INDICATORS IN ELECTROSHOCK: For more than a year, Dr. Karliner of the attending psychiatric staff has been interested in formulating some prognostic factors which would be helpful in electroshock. Discussions were held in June and at the suggestion of Dr. Miller, Dr. Karliner prepared a special scale to evaluate prognosis. This scale will be presented to the Research Committee and assessed over the next six months.

C. STAFF CHANGES:

Dr. Joseph Jaffe, a practicing psychoanalyst, was appointed to the Research Service as research assistant in psychiatry, and began work on September 1st. Dr. Jaffe's interest is in the behavioral and language changes which are induced by altered brain function and the relation between such changes and premorbid personality.

During this period our space problem were resolved effectively by the extension of the laboratory on the first floor of the Lowenstein building. Our equipment problems have also been reduced. The tachistoscopic equipment was brought into alignment and works well. We are now able to present tachistoscopically two pictures individually or simultaneously. The electric stimulators are functioning satisfactoraly so that we are now able to produce isolated simultaneous square wave stimuli with the ability to vary any of the essential parameters.

D. FUNDS:

In May, we submitted an application to the United States Public Health Service for support of Dr. Jaffe's program. In September, Dr. Jerome Frank came to the hospital and interviewed the staff in an evaluation of our program. We anticipate a response from the USPHS in mid-December. In June, we also submitted the necessary forms for second year renewal grants both for Dr. Goldenberg and myself, and both renewals were approved. It is important to note that for both these renewals, the overhead allowances were increased to 15%.

At the suggestion of Mr. Coleman, specific protocols of our research program were submitted to the Kaufman, Hoffheimer, and Ittleson Foundations during this period.

The protocol which the Research Service has been writing for the Ford Foundation grant program was submitted to the Research Committee of the Medical Board in September. It was the consensus that the protocol was unsatisfactory and that it not be submitted. Following their suggestions, changes are being made by the Research Service with the cooperation of Drs. Lenzer and Luttrell.

At the present time, I am planning to submit another application to the USPHS in January for consideration at their March meetings for renewal of our present program. I am also contemplating an application to the Foundation Fund for Psychiatry for support for the ambivalence study, as soon as the basic work is completed.

E. OTHER ACTIVITIES:

1. ISRAEL STRAUSS VOLUME OF THE JOURNAL OF HILLSIDE HOSPITAL: Following discussion with Dr. Tarachow, the Research Service has undertaken the necessary secretarial and editorial work in assisting Dr. Tarachow in issuing the special Commemorative Volume of the Hillside Journal.

2. ISRAEL STRAUSS LECTURE: Consideration is being given by members of the Israel Strauss Lecture Committee for the next lecture. Discussion is at present centered about a number of candidates and a final decision should be available by the end of November.

Respectfully submitted,

MF:gw

Max Fink, M.D.
Director of Research

Department of Biochemistry ..... Dr. H. Goldenberg

Research Progress Report, November 1955

Major Work in Progress

1. Chlorpromazine Studies

Our previous work has been summarized in the report for the 6 month period ending Oct. 1955. We have subsequently learned from two representatives of the Smith, Kline and French Laboratories that Drs. Salzman and Brodie, working at the National Institutes of Health, have identified chlorpromazine sulfoxide in the urine of dogs and men after treatment with chlorpromazine. A sample of the sulfoxide was requested from Smith, Kline and French and arrived the end of Nov.

The ultraviolet absorption spectrum of the sulfoxide was determined in aqueous solution and compared to the spectrum obtained with extracts from patients' urine. A remarkable similarity was noted. On the basis of this and other data accumulated in our lab., there can be no doubt but that urine from mental patients receiving chlorpromazine contains: (1) chlorpromazine, (2) the sulfoxide, (3) one or two other alkaloids of related structure, and (4) at least one break-down product which yields a violet color with sulfuric acid, as contrasted to the pink colors typical of chlorpromazine and its sulfoxide.

Using our dye-partition scheme, the sulfoxide yields a color which is roughly 1/5 the value given by chlorpromazine in equimolar concentrations. Hence our dye scheme is not applicable as such to the analysis of fluids containing both derivatives, unless some additional information is available on the relative amounts present. Fortunately the relative proportions can be estimated from the extent to which the color is depressed by the addition of ether. Nonetheless, we are withholding a manuscript dealing with chlorpromazine analysis until this question is completely resolved.

Ultraviolet and chromatographic studies are to be undertaken soon to establish the various chlorpromazine derivatives in urine and their clinical significance.

2. Role of Toxic Agents in Mental Disease: An Enzyme Test for LSD

The first draft of a manuscript entitled "Inhibition of Serum Cholinesterase by Lysergic Acid Derivatives. Submicro Detection of LSD 25" has been completed. Copies are to be forwarded to the Research Committee on Dec. 8th.

3. Steroid Hormone Conjugates

Little progress has been made in this area in the last 6 weeks because of a delay in construction of our chromatography cabinet and unavailability of electrical parts needed for the circuit. This situation should be remedied by the middle of December.

cc. to: Dr. M. Fink
Dr. Jos. S.A. Miller

ELECTROSHOCK THERAPY EVALUATION PROGRAM

from the

Research Service of the Hillside Hospital

Glen Oaks, New York

December 20, 1955

Alvin E. Coleman, President

Joseph S.A. Miller, M. D.
Medical Director

Electroshock Therapy Evaluation Program

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I. AIM:

During the past few decades there has been an intensified development of various new somatic therapies for mental illness. While some have eventually fallen into disrepute, electroshock therapy has been established as an important and successful method for both immediate and long term results (1). Despite its empirical usefulness, the many theories concerning the mechanism of this therapy have been either disproven or are so vague that their validity cannot be tested. In a comprehensive review, Kalinowsky and Hoch (2) emphasize the lack of information in this regard stating: ".....the theoretical aspects of the various somatic treatments ..... are poorly understood, or, as in the case of the shock treatments, still entirely obscure in their mode of action."

The aim of this program is to study the therapeutic mechanisms in electroconvulsive therapy by the systematic investigation of behavioral, personality, physiological and biochemical factors. While the program has electroconvulsive therapy as its focus, considerable theoretical and experimental information can be derived to relate the phenomena observed in this therapy to other somatic treatments such as lobotomy, electronarcosis and insulin coma.

II. BACKGROUND:

The use of electroconvulsive therapy has stimulated an abundance of hypotheses (3) and much research. Both the kind of theories and the experimental investigations undertaken, however, reflect the particular interest of the investigator and his theoretical frame of reference regarding the origin of mental disorders. Thus, each has been usually limited to one aspect of the problem. In general, these theories may be differentiated between those that emphasize physiological, biochemical, or psychological constructs.

A classical physiological construct is exemplified by Gellhorn (4) who suggests that the various forms of shock therapy "act on the centers of the autonomic system, produce intensive and prolonged sympathetico-adrenal discharges and alter, through augmented hypothalamic-cortical activity, mental processes and behavior." The varying responses of blood pressure, heart rate, psychogalvanic reflex, and other physiological indices to chemical stresses are interpreted as indices of sympathetic reactivity. Much data has been obtained to show that electroshock therapy induces a change in this autonomic reactivity, and recent studies by Funkenstein and his co-workers (5) support this conclusion.

Much biochemical study has been devoted to the relation between mental illness and steroid metabolism. Numerous instances (6) in which a relation between ketosteroid excretion rates and change in mental state following electroshock therapy are reported, but the clinical difficulties in the measurement of steroids have left this issue unresolved. More recent studies exploring the relationship between individual steroids to the total excretion rate (7) utilize elaborate chromatographic separation technics.

In a good review of the biochemical and neurophysiological hypotheses, Ashby (8) presents experimental evidence to justify the view that the mode of action of electroconvulsive therapy is through effects on the adrenal cortex mediated by direct stimulation of the hypothysis.

Psychologic constructs generally fall into three designs - studies of the psychic significance of the loss of consciousness; the relative importance of memory loss; and an estimate of the subject's re-integrating abilities following a period of confusion. Numerous studies emphasize the unconscious significance of the treatment as a "rebirth which eliminates regressed narcissism" (9); or a satisfaction of a need for punishment and expiation for committed sins (10).

Amnesic effects are a common concomitant of treatment but most studies emphasize the temporary nature of the impairment. The significance of these defects for therapeutic results is emphasized by numerous authors. Data is presented to show that treatment reduces the emotional charge on the patient's associations (11), induces a loss of familiarity for emotionally-toned associations (12), or a selective forgetting of unpleasant life memories (13).

These constructs are further elaborated by authors who believe that the induction of an organic confusional state including behavioral responses as euphoria, impulsiveness or over-reacting is the basis for electroshock improvement (14). A more recent elaboration of this explanation is that enumerated by Weinstein & Kahn (15), described subsequently.

Another group of psychologic explanations regard changes in adaptive processes as the basic therapeutic mechanism. Frosch and Impastato (16) describe electroshock as causing a dissolution of the ego which then re-integrates on a previous or higher level of adaptation. Alexander has a similar opinion suggesting that electroshock arouses and enhances active defensive operations. For this reason he asserts that such therapy is most effective in those conditions in which such operations are at a low ebb, as in depressions, but are ineffective in conditions in which defensive operations are already highly alerted (17).

Another hypothesis was developed by Weinstein and Kahn (15) in which two aspects of the therapeutic process were related. They asserted that the therapeutic action of induced convulsions lay in the creation of a milieu of altered brain function in which the patient's symbolic expression of his problems is altered, particularly in the form of explicitly denying them. Their studies, documented by an extensive neurologic experience with patients with cerebral dysfunction, amply demonstrate a great variety of changes in adaptive behavior. They describe altered patterns in language (18), orientation (19), attention (20), sexual behavior (15b) and awareness of defect (21) as manifestations of adaptive behavior and conclude that these mechanisms constitute the patient's attempt to deny his illness or its meanings. Such attempts at denial were most striking and enduring in those patients who had habitually used the defenses of verbal denial and rationalization as a means of coping with their problems (22). They also demonstrated that these patterns indicative of "denial" could be elicited in an interview following the intravenous administration of sodium amytal when they were not manifest in the clinical interview (23).*

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* This appearance of patterns of disorientation and explicit denial following the administration of sodium amytal is so clearly associated with diffuse cerebral dysfunction, that it has been described by these authors as a test for such dysfunction (23). This has been named the "amytal test."

Thus, when they noted a direct relationship between a patient's denial of pain following electroshock therapy and the appearance of the signs of cerebral dysfunction (positive amytal test) they suggested that the mechanism of electroshock therapy may be the facilitation of patterns of denial by altered brain function (15).

This hypothesis is an attempt at integrating physiological and psychological factors. As such, and in view of the operational terms in which it is stated, it has provided a theoretical base upon which our studies have been elaborated.

III PREVIOUS STUDIES:

For the past three years, studies investigating manifestations of altered cerebral function in psychiatric patients, have been in progress at Hillside Hospital. In 1952, the application of the amytal test to psychiatric subjects was assessed (24). Positive responses were found only in patients who had had electroshock therapy or had other indications of organic brain disease.

During 1953-1954* in order to test the relationship between altered brain function and the response to electroshock therapy, consecutive patients referred for treatment were tested at weekly intervals with serial electroencephalograms, amytal tests, simultaneous tactile perception** tests, and tests of recall function.

A marked correlation was found between improvement following electroshock therapy and early, persistent and severe changes in both the amytal tests and the electroencephalograms. If such changes did not appear, improvement failed to occur. In contrast, no such correlations were manifest between improvement and tests of recall function or changes in simultaneous tactile tests.

Twenty-four subjects were tested in this first study, and were classified independently by the supervising psychiatrist as markedly improved (11), moderately improved (6) and unimproved (7) at the end of one month post-treatment.

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* Aided by a Fellowship from the National Foundation for Infantile Paralysis (Dr. Fink, 1953) and Grant M-927, National Institute of Mental Health, National Institutes of Health 1954-56.

** Previous studies of the perception of two simultaneous tactile stimuli demonstrated characteristic patterns of failure to perceive or localize one of the stimuli in patients with diffuse cerebral dysfunction (25).

Of the markedly improved patients, every one had at least one positive amytal reaction during treatment. Of the 50 tests given to this group, 38 (76%) were positive. In contrast, of the unimproved patients, five of the seven never showed a positive result, and of the 45 tests administered to this group, only 6 (13%) were positive. The moderately improved group showed more positive responses than the unimproved patients, but fell far short of the much improved group.

In addition, there were consistent changes in language and non-verbal aspects of behavior indicating alterations in adaptive mechanisms in the much improved group, even in interviews not employing amytal. These alterations were either minimally or only transiently manifest in the unimproved group and then only under the influence of sodium amytal.*

Concomitant studies of the electroencephalograms taken on a day preceding the amytal test indicate a similar relationship. The 160 records were first measured for per-cent time slow wave (delta) activity, the extent of burst activity and the amplitude and frequency of the slowest waves present. They were then placed in a rank serial order. Those falling in the upper third were labelled "high abnormality" and those in the lower third as "low abnormality." Of the much improved patients, 25% showed a high degree abnormality after one week of treatment; 80% after two weeks and over 90% after three weeks. In the unimproved patients, however, none had a high degree abnormality record during the first three weeks and only one had such a record by the fourth week of treatment. The records of the moderately improved patients fell between these two groups.**

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* Presented at the Annual Meeting of the American Psychiatric Association, May 10, 1955.

** Presented at the joint meeting of the Eastern and Southern Electroencephalographic Societies, Bethesda, September 30, 1955.

Changes in memory and learning were tested in these subjects by using the principle of retroactive inhibition. By the serial testing of recall of 3-letter originally learned words following the interpolated learning of nonsense syllables, patterns of decrement in learning and recall were elicited. As a group, the patients showed increasing impairment up to the third week of treatment, and a rapid improvement after the cessation of treatment. No relationship, however, could be established between impairment and response to treatment.*

The responses of these subjects to simultaneous tactile tests using touch stimuli were also assessed. While an increasing impairment in the ability to identify and localize the two stimuli could be demonstrated with increasing treatment, no relation to improvement was noted. The tests were extremely gross, however, and in anticipation that more meaningful correlation for this index of altered brain function could be obtained, a study using threshold electrical stimuli has been undertaken (pg. 10).

As a result of these studies, it was our conclusion that early, persistent and severe changes in both the electroencephalogram and in the amytal tests are a necessary, though not sufficient pre-requisite for improvement following electroshock therapy. These observations make it possible to predict the short term response to electroshock, and such a study was undertaken earlier this year (pg.11).

Concomitant with these studies, we have made some preliminary observations in patients undergoing insulin coma therapy. Recent reports of the value of prolonged coma as the basis for improvement (26) have been confirmed in our patients. In one unusual case report we noted a direct relationship between

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* Presented before the Electroshock Research Association, May 8, 1955 and awarded their Annual Prize Award for excellence in research design.

altered brain function, altered patterns of adaptation in language and behavior, and clinical improvement (27).

Concurrent with these psychologic investigations, basic studies have been done in biochemistry. The biochemical research laboratory was established in 1950* with an initial program of study of the relationship between steroid excretion patterns and states of mental illness.

The studies, utilizing alumina column chromatography, demonstrated atypical urinary ketosteroid levels in a number of psychotic patients. The excretion of B-steroids (particularly dehydroisoandrosterone) was found to be elevated, and the etiocholanolone was depressed (7a). The 11-ketoetiocholanolone values appeared to be sex-dependent: male patients excreted the steroid metabolite in normal amounts, while the several female patients studied had markedly elevated values.

During the past year, a collaborative study was initiated with the biochemical department of the Sloan-Kettering Institute of New York. Similar steroid excretion pattern studies were undertaken utilizing paper chromatographic technics. In the first phase of the study recently completed, the elevated excretion of 11-ketoetiocholanolone was confirmed, with a severe reduction in the excretion of this compound prior to discharge, at a time when the patient had shown considerable improvement from her illness.

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* Supported by grants from the Dazian Foundation for Medical Research.

IV. STUDIES IN PROGRESS AND IN DEVELOPMENT:

1. Relation of Tests of Altered Brain Function to Improvement:

Our earlier studies have shown a direct relationship between altered brain function and response to treatment. It is apparent, however, that this relationship holds for certain indices of altered brain function only and not for others. Further study, therefore, has been undertaken to confirm and elaborate these findings, as well as to investigate methods of measuring cerebral function which are more reliably related to clinical improvement.

a. Amytal Test and Electroencephalogram:

Amytal tests and electroencephalograms are done in all subjects before, and during the second and third weeks of electroshock treatment. On the basis of our earlier findings the data is used to make a prediction of the short term response to treatment. It is predicted that those patients with a high degree electroencephalographic abnormality and with positive amytal test findings will be most likely to show improvement; while those with a low degree electroencephalographic abnormality and with negative amytal results are considered unlikely to improve.

b. Tactile Perceptual Tests:

As described before, the simultaneous tactile perceptual test results in our first series of patients were inconclusive. It was planned to repeat this study using threshold electrical stimulation, under conditions wherein the various stimulus parameters could be rigidly controlled. Under terms of an existing USPHS grant (M-927) an instrument assembly consisting of two Grass S4-B stimulators monitored by an oscillograph was devised which can deliver independent square wave electrical stimuli. Using this assembly, the patients are tested for their ability to perceive two stimuli applied simultaneously to different parts of the body. By applying this refined technique

it is anticipated that changes in brain function not otherwise apparent may be elicited. These observations will be compared to the degree of improvement and to our other test-results. As in the case of the electroencephalogram and amytal tests, patients are tested before and at stated intervals during the course of treatment.

c. Memory Tests:

Numerous theories of the relation of memory loss and improvement have been described. Our own data to date shows no significant relationship between the memory loss for nonsense syllables and simple words and improvement. But there is considerable evidence that there is a selective forgetting, during treatment, of significant life situations and memories. For this purpose, a record is made of events during the preceding six months which may be of emotional significance to the patient. During treatment, inquiries are made of the patient's recollection of these events, verbatim records made, and these compared to the pre-treatment reports.

2. Relation of Premorbid Personality to Duration of Response:

It has also been apparent that the relationship between altered brain function and clinical response is valid only for the short term response to treatment, i.e., several weeks after treatment. When followed for a six month period, several of the improved patients had relapsed, showing a return of their former symptoms, and in some instances requiring further hospitalization. To account for the varying duration of clinical response, the hypothesis was advanced that the difference was related to differences in premorbid personality patterns. Specifically, it was suggested that patients who showed the characteristics of the "explicit verbal denial personality" (22) would be those more likely to maintain improvement.

The premorbid personality of each patient is assessed by four procedures - an interview with family members, psychologic tests, tachistoscopic tests and psychiatric interviews.

a. Family Interviews:

At least two close relatives are seen in independent interviews. A standardized questionnaire has been devised to elicit characterological factors indicative of the "explicit verbal denial" personality. For this study fifteen characteristics defined as typically present or absent in this type of personality were selected. Such items include prestige consciousness, sensitivity to criticism, imagination, temper and attitudes to sex and illness. Each patient is rated on a scale of 0 to 2 for each item - the higher score signifying a greater tendency to denial.

b. Psychologic Tests:

Each patient is tested on a standard psychologic evaluation battery including the Rorschach and Thematic Apperception Tests. These tests are assessed for character structure and usual types of defense or adaptation. Such tests are repeated at the termination of the treatment program and again prior to discharge, to obtain additional information as to changes in behavior in the course of treatment.

c. Tachistoscopic Tests:

A tachistoscopic study has been devised, in which pairs of emotional and non-emotional words are flashed on a screen at 10, 20, 50, 100, and 250 millisecond periods. The patient's ability to identify the words, the reaction time, and the distortions are ascertained. This pre-treatment data is now being explored as to its ability to clarify the patient's usual defense patterns. The tests are repeated at the end of treatment and again prior to discharge for the possibility that characteristic changes in perception develop with altered modes of adaptation.

d. Psychiatric Interviews:

In the course of estimating changes in behavior, patients are seen prior to treatment, and at intervals during treatment. In a clinical interview setting, an assessment is made of the patient's symptoms, and usual modes of adaptation. Changes in symptoms, behavior, language and modes of adaptation are noted. By interviews with the patient's therapist, judgment as to the significance of such changes and their relation to treatment, or altered cerebral states can be made.

On the basis of the data in a-d above a prediction of response to treatment is made. Prior to the start of treatment the patients are classified as:

1) those unlikely to improve;

2) those likely to improve moderately or temporarily;

3) those likely to maintain marked and sustained improvement (for at least six months).

During the third week of treatment, (after the patients have had 7-9 treatments), a second prediction of the short term response is made according to the change in the physiological indices.

3. Altered Patterns of Adaptation Manifested in Verbal and Non-Verbal Behavior:

In the earlier study on the amytal test it had been noted that specific changes in language and behavior indicative of altered adaptive responses occurred in the improved patients to a significantly greater degree than in the unimproved patients. Further experimental procedures were deemed necessary to clarify the nature and significance of these changes.

a. Language Changes Induced in Amytal Tests:

The amytal test procedure is recorded. This is a highly structured interview situation, and systematic observations are made of the patterns of language. The hypothesis tested is that those patients who show consistent, increasing use of the following types of adaptive language will be more likely to improve: 1) The use of the second or third person. In such instances the patient reports his main trouble as "the Doctors say I'm depressed", or state the wish that "my family should be well." 2) The selective response to questions, as answering readily questions about date and location but failing to answer, mumbling or using neologisms when asked about illness. 3) The use of conditional or qualifying expressions, or the subjunctive mood which has the effect of vitiating the patient's committment to the statement. An example is "sometimes I feel kind of depressed", in w hich "sometimes" qualifies the temporal degree of illness, and "feel" and "kind of" qualify the intensity of the illness. Committment would be indicated by the direct, unconditional statement of "I am depressed". 4) The use of cliches or stereotyped expressions in discussing illness, as "to tell you the truth..." or "Well, in a manner of speaking..." or "I didn't keep my shoulder to the wheel". 5) Language filled with non-sequiturs, circumlocution, ornate or pedantic statements. 6) The use of humor when talking about their illness or other problems. 7) The use of metonymy or paraphasia, as referring to the examining Dr. as a "recorder". 8) The various forms of explicit denial including confabulation about the main problem and temporal displacement. 9) Changing the symbolic frame of reference in response to questions, as replying to the question, "how do you feel?", by stating, "with my hands." 10) The use of hyperbole, as "you're the best Dr. in the whole eastern Atlantic seaboard area."

b. Language Changes in the Post-Shock Confusional State:

Each patient is tested for orientation and awareness of his main problem in the period of awakening immediately following a treatment. This is done after the initial treatment and then at weekly intervals. At such times, the neurologic cerebral defects are most severe, and a variety of adaptive changes in the pattern of language appear. These may be comparable to the language changes noted in the other interview situations, and the records are assessed for prognostic indications both as to the later language changes and the degree of improvement.

c. Sentence Completion Study:

A way of studying the patterns and changes in language in a quantitative fashion has been devised using a sentence completion technique. The patient is given 40 sentences to complete, which have been structured according to four different patterns. Ten of the sentences have been put in the first person, unconditional, such as "I wish that.....", "I am criticized when....", etc. Ten others are identical in meaning except that they are expressed in the third person and with a conditional or qualifying aspect, as "people sometimes wish that.....", "people are usually criticized when.....," etc. In the remaining twenty items no person is specifically indicated. In ten of these sentences, however, the sentence is direct or refers to an exact occurrence or event as "every time....", "when the doctor comes in.....", etc. The remaining ten have a conditional, qualifying or indefinite aspect, as "at times....", "things usually seem a little better when.....", etc.

The response of patients to the incomplete sentences is not analyzed for content in the traditional psychologic manner. Instead, each response is rated

for its grammatical or syntactical structure. The ratings include whether the response is in the first, second or third person, is direct or conditional, or manifests aspects of language described above (page 14).

This study is based on the following assumptions: 1) A sentence which begins in a manner most obviously applicable to the patient (e.g., first person, unconditional) creates maximum stress and is most likely to elicit adaptive responses. 2) A sentence which is expressed in the third person or is conditional is less applicable to the patient. It creates minimal stress and is least likely to elicit adaptive responses. 3) The syntactical person used to complete a sentence whose beginning is indeterminate in regard to person is indicative of the degree of stress experienced (e.g., the use of the first person shows less defensiveness, the use of the second or third person shows greater defensiveness).

d. Attitude Interviews:

In this part of the study an attempt is made to define operationally the adaptive mechanisms of the ego. Two structured interviews are held, in which the same questionnaire is followed. The attitude of the examiner, however, is reversed from one interview to the next. In one interview the examiner is empathetic, pessimistic, concerned, and in the other interview he is brusque, non-empathetic, insensitive and tends to minimize the patient's difficulties. In general, the first attitude produces good rapport with these disturbed patients, while the latter results in a grossly non-communicative situation. Although the same questions are asked in each interview, the wording is altered to be appropriate to the examiner's attitude. In one interview he asks such questions as "feeling poorly today?", "You must consider your condition pretty serious?", and "has it been getting worse?." While in another interview he asks, "feeling pretty well today?", "you don't consider your condition serious, do you?" and "have you been improving?".

The two structured interviews are performed just prior to electroshock treatment and repeated following the course of treatment. All interviews are recorded. There are two variables in the study: 1) alteration of the patient's behavior by treatment, and 2) alteration in the examiner's attitude. The four recordings are studied for content, vocal changes, and language changes. The defensive mechanisms of the patient and any changes in it can be defined, operationally, in terms of the range of transactions that can be carried out both before and after treatment. For example, a very depressed patient may be communicative before treatment in the concerned, empathetic interview, whereas he will be unable to participate in the examiner's mood when the latter is jovial, bantering and minimizing. However, if his response to treatment is one of euphoria, the situation may be reversed. Following treatment he becomes suspicious, hostile, or anxious when the examiner is concerned and empathetic, whereas communication is less stressful in the optimistic interview. Thus the change in the defensive system of the patient can be stated in objective terms, i.e., in terms of his reactions to a standardized range of interpersonal situations.

4. Clinical Ratings of "Improvement":

These various experimental and test methods of evaluating changes in language and behavior may have further significance in the psychiatric rating of "improvement." In our previous studies, we experienced considerable difficulty in rating our patients. Is symptomatic relief to be the guide? Or, is a "social recovery" or "social improvement" to be the goal?. Is recovery to be judged by the degree of insight as well as symptomatic relief? Agreement by psychiatrists in the definition of "recovered", "much improved" and "unimproved" is not available, and yet, this issue is crucial to further investigations. We

have therefore undertaken the further task of assessing these terms as they apply to the electroshock population.

Central to this problem of evaluation are the degree and type of incapacity of the patient, his premorbid personality, the goal of the therapist, and the patient's attitudes to therapy. Other aspects, as intercurrent events, capacity of the therapist, temporal suitability of therapy, the patient's environmental assets are also important to assessment, but are not emcompassed at present. To clarify the meaning of "improvement", the following evaluation studies are in progress.

a. Pre-treatment Evaluation:

Patients are referred for electroshock therapy by the supervising psychiatrist and resident therapist. An independent psychiatric evaluation is made by the research psychiatrist. Two aspects are specifically encompassed in this study: 1) the symptoms and clinical signs of decompensation which are recorded in a descriptive mental status and rated for degree of symptomatology on a Malamud rating scale (28); 2) an estimate of the patient's level of ego development with a description of his usual defensive operations.

b. Changes in the Therapist-Patient Relationship:

In interviews with the resident therapist held prior to the onset of electroshock therapy, the relationship between the therapist and the patient are explored with specific emphasis on the reason for the recommendation for this form of therapy, the goals of the treatment, and the patient's attitude to the treatment. Since the primary method of treatment of mental disorders at this hospital is psychotherapy, the recommendation for electroshock generally carries with it the assumption that communication between the patient and therapist was no longer meaningful. For this reason, the exploration is devoted to those changes in the relationship that led to the recommendation, and

a definitive statement of those aspects of behavior and symptoms that it is anticipated the treatment may affect. We are also interested in the therapist's attitude to this form of treatment, and attempt to assess the role this attitude may play in the eventual results.

Furthermore, there are numerous theories relating the results of the therapy to its punitive aspects, and in our inquiries, attempts are being made to assess the significance of this factor in the outcome. During the interviews with the resident therapist and with the patient, the patient's attitude to the treatment, his defensive operations (both language and behavior) against the reality threat that electroshock represents, and the alterations in his attitude during the weeks of treatment are studied. Further information regarding the significance of this factor will be ascertained in the course of our control study (page 21).

c. Follow-up Study:

Crucial to the evaluation of "improvement" is the opportunity to repeat evaluations at various periods following the period of treatment Recently, a four-year follow-up report of the patients discharged from this hospital was made available (1) and this indicated the customary disparity between discharge ratings and eventual course of the illness. In the course of this investigation, repeat evaluations by the same observers is being carried out at various times during hospitalization and six months after treatment. As a check on the predictions made on the basis of the personality and the physiological factors studied, specific follow-up evaluations are recorded for the two-week post-treatment period (short-term result) and the six months period (long-term result). These evaluations are compared to the ratings of the resident therapist, supervising psychiatrist and the medical director. In each instance, the ratings made in this study are formulated in terms of the projected and actual changes noted in those aspects of behavior, language and interpersonal

communication previously interpreted as being indicative of defensive operations.

5. Relation of Steroid Excretion to Improvement:

The studies of the patterns of excretion of steroids and their relation to mental states, described on page 9, is continuing. More recently emphasis has been on the development of techniques for the measurement of steroid conjugates. During the past year * new separative and colorimetric techniques have been devised (29) to measure steroid sulfate compounds in blood and urine. Daily urinary excretion patterns for these compounds are essayed prior to treatment, during the course of electroshock and again prior to discharge in selected patients. The object of this program is to resolve the sulfate - bound steroids, and compare these values with the total individual hormone levels. Besides elucidating the relationship between hormone excretion rates and states of mental illness, such studies indicate the extent to which the liver (30) participates in the metabolism of steroid hormones.

6. Effect of Autonomic Functions on Results of Electroshock Therapy:

In the course of our electroencephalographic studies, it has become apparent that a number of patients fail to show the typical alterations in cerebral rhythms despite extensive treatment. These patients also fail to show changes in the amytal tests, simultaneous tactile tests, and frequently evince no confusional periods. Simultaneous with these studies, the reactivity of the blood pressure and the pulse rate to the administration of mecholyl (the "Funkenstein-test") have been carried out. This, too, was done prior to treatment and immediately after the course of treatment had ended. Marked variations in the responses to this medication were found in these two test periods. These observations followed in a general way the reports of the earlier workers, but we are now undertaking the exploration of the relationship between the alteration in tests of altered brain function and these physiological tests.

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* Aided by a grant (A-675C) from the National Institutes of Health, United States Public Health Service.

V. THE PROJECTED PROGRAM: SUMMARY -

1. Method:

The projected program is a continuation and development along the lines indicated in the preceding two sections of this report. Our ultimate goal is to clarify the mechanism of electroshock therapy by the systematic and integrated investigation of the inter-relationship of behavioral, personality, physiological and biochemical factors.

This program is being undertaken by a full-time interdisciplinary research staff consisting of psychiatrists, psychoanalyst, neurophysiologist, physiologist, experimental psychologist, biochemist and allied technical help.

Some of the specific studies in the program are already clear in scope and outline. Others will become apparent as the program continues and new critical problems appear or further promising leads develop. Two new basic methodological aspects have already been decided upon.

1. Control group: One of the major deficiencies in our work to date has been the absence of an adequate control group. Accordingly, starting January 1, 1956, patients referred for electroshock will be divided into two groups in a random fashion. One group will receive the usual course of convulsive therapy; the other group will be given sub-convulsive treatments. This recommendation follows the recently reported instructive study of Ulett et al. (31). In other respects the two groups will be treated in the same fashion. The only person who will know which patients are in each group will be the supervising psychiatrist administering the treatments. The purpose of such a control group is to differentiate the physiological effects of the induced convulsions from other factors affecting the therapeutic outcome. Some of these factors might include 1) the nature of the particular disease process, as schizophrenia or involutional depression, etc.; 2) the attitude and symbolic meaning of the treatment to the patient; 3) the special attention of a large

numbers of observers incident to being placed on the treatment program; 4) the attitude of the patient's therapist toward the patient and toward electroshock therapy, including the expected goals in each case; and 5) the relative effectiveness of other forms of therapy provided for these patients in the hospital milieu. The use of a control group will also clarify the nature of "spontaneous recovery" and may aid in the understanding of "atypical" results in the patients actually receiving convulsive therapy.

2. Insulin Coma: It is planned to extend the present methods of study to an investigation of those patients receiving insulin coma therapy.

2. Significance

This program of study has both applied and theoretical significance. It can lead to the improved clinical use of electroshock therapy since there will be a greater understanding of the therapeutic mechanism. It will be possible to select more skillfully those patients who will improve, to better manipulate other factors involved in the therapeutic process, and to predict more accurately future management problems.

This study also leads, however, to a greater understanding of the psychopathology of mental illness. Through the various methods of study a clearer picture of the mechanism of defense and modes of communication will be obtained which may contribute more operationally accurate and meaningful criteria for diagnostic classification and for the determination of "improvement".

Finally, the investigation may throw light on other therapeutic techniques. The studies of the alteration in cerebral function and the observations on the relationship between behavior and cerebral damage have significance for the studies in lobotomy and cerebral electrocoagulation. It is also likely that the insights gained here into the changes in language and modes of adaptation may make possible an eventual significant study of psychotherapy.

VI. FACILITIES AVAILABLE:

1. Hillside Hospital is a 200 bed non-profit psychiatric hospital. All admissions are voluntary, with periods of hospitalization varying from 4-12 months. All patients are available for study.

The hospital was established in 1927, for the purpose of treating ambulatory psychiatric patients. A residency training program was instituted early, under the supervision of an active staff of psychoanalytic psychiatrists. In 1950 the research biochemical laboratory was established, to be followed in 1953 by the neurophysiological research laboratory.

In 1954 these laboratories were combined and expanded, and a Research Service established as a full-time operation of the hospital. A full-time Research Director was appointed to integrate all the studies into a basic program. At this time, the staff consists of the Director, research assistants in psychiatry and psychology, biochemist and assistant biochemist, physiologist, and EEG technician. In addition, a psychologist and two chemists are associated on a project basis.

Laboratory facilities include: (a) Electroencephalographic unit with a Medcraft D-8, 8 channel instrument; (b) Neurophysiological laboratory with two S-4B Grass stimulators, Du Mont # 340 R oscillograph; two synchronized tachistoscopic projectors and auxiliary electronic equipment; (c) Biochemical laboratory with 1000 square feet of laboratory space and equipped with the following major items: Beckman spectrophotometer, Warburg respirator, Coleman spectrophotometer, and radioisotope unit following the basic specifications of the A.E.C.

2. Personnel:*

(a) Dr. Max Fink, M.D., Director of Research: Undergraduate studies were undertaken at the University College of New York University, and the degree of B.A. cum laude with Honors in Biology was granted in 1942. He attended the New York University College of Medicine, graduating in 1945. After a rotating interneship he served in the U.S. Army, where he graduated from the School of Military Neuropsychiatry in 1947, and was Chief of the Psychiatric Section, Fort Knox Station Hospital during 1947.

Formal neurologic training was received at Montefiore Hospital in New York (1948-1949) and at Bellevue Psychiatric Hospital (1949-1951). Formal psychiatric training was undertaken at Bellevue Psychiatric Hospital (1950) and then at Hillside Hospital (1952).

During 1951, and again in 1953, he was a research fellow of the National Foundation for Infantile Paralysis. Both periods of study were under the direction of Dr. Morris B. Bender, first at New York University College of Medicine and then at Mount Sinai Hospital in New York.

In 1952, he was certified in Neurology, and in 1954, in Psychiatry, by the American Board of Psychiatry and Neurology. Simultaneously he attended and graduated from the William Alanson White Institute of Psychoanalysis, Psychiatry and Psychology, receiving their Certificate for Physicians in January, 1953. In June, 1954, he was granted a research grant of the National Institute of Mental Health for a 2-year study of electroshock processes. In September, 1954, he was appointed Director of the Research Service at Hillside Hospital. Dr. Fink is 33, married and has one son.

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* Bibliography of personnel is appended, page 38.

(b) Dr. Joseph Jaffe, M.D., Assistant in Psychiatry: Following undergraduate studies at Columbia College (B.A., 1944), Dr. Jaffe attended the New York University College of Medicine, and was granted his M.D. in 1947. Then he was elected to Alpha Omega Alpha. Following a rotating interneship, he began three years of study at the Bellevue Psychiatric Hospital. First as a resident in psychiatry, then in neurology, he completed his studies as a U.S.P.H.S. post-doctoral research fellow under the supervision of Dr. Morris B. Bender.

From 1951, to 1953, he was in the United States Air Force, graduating from the School of Aviation Medicine. He was Chief Psychiatrist at the Mitchell Air Force Base Hospital.

Since discharge from the military service he has been in the private practice of psychiatry. He was certified in psychiatry by the American Board of Psychiatry and Neurology in 1953. Since 1949, he has been a candidate in psychoanalysis at the William Alanson White Institute of Psychoanalysis, Psychiatry and Psychology and for the past two years has been a Research Assistant at the Mount Sinai Hospital of New York. He was appointed to his present position in September, 1955.

(c) Dr. Harry Goldenberg, Ph.D., Chief Chemist: A graduate of the College of the City of New York in 1944, he was the recipient of a Tremaine Scholarship and graduated cum laude. Dr. Goldenberg received his Ph. D. in 1949 from the Polytechnic Institute of Brooklyn. He has been an instructor in biochemistry at the Polytechnic Institute (1946-47) and at Brooklyn College (1951 to date). In 1947-49 he was a Research Fellow in enzymology of the National Institute of Health, and from 1950 to 1952, he was a chemist to the U.S.P.H.S. project at the Jewish Hospital of Brooklyn studying enzyme methods in clinical chemistry.

(d) Dr. Robert L. Hahn, Ph.D., Assistant in Psychology: After graduation from Brooklyn College in 1940, he undertook graduate studies at Columbia University. These studies were interrupted by four years of service in the United States Army, where he went to Clinical Psychology School and served as psychologist in various hospitals in this country and overseas. On leaving the army he became Research Psychologist in the Department of Neurology of the Mount Sinai Hospital in New York, where he worked under the supervision of Dr. Morris B. Bender and Dr. E. A. Weinstein until January, 1955. He is the author of numerous experimental studies, and is co-author of the monograph, "Denial of Illness: Symbolic and Physiological Aspects" published in May, 1955.

He received his Ph.D. from the New York University School of Graduate Arts and Sciences in 1953, and was an instructor of psychology at Brooklyn and Hunter Colleges for two years. For the past two years he has been a consultant to the New York State Department of Mental Hygiene and has conducted training programs in several of the mental hospitals. Since January, 1955, he has been a member of this staff.

(e) Dr. Hyman Korin, Ph.D., Assistant in Psychology: Following four years of military service, he matriculated at College of the City of New York and received his B.S. in 1949, and his M.S. in 1950. During 1951-52 he was psychology interne at the Mount Sinai Hospital and matriculated for his Ph.D. at New York University. Since June, 1953, he has been Research Assistant in Psychology at Hillside Hospital. He recently completed his doctoral thesis on "The Effects of Electroshock on Retroactive Inhibition," and received his Ph.D. in October, 1955.

(f) Dr. Arnold Blumberg, M.D., Internist: Dr. Blumberg received his M. S. from the University of Pennsylvania in 1942, for studies in physiology, and in 1945, received his M.D. from the New York University College of Medicine. Following a rotating interneship and two years of military service, he continued his residency training at Goldwater Memorial Hospital from 1948 to 1952. First

as a resident in neuropsychiatry, then as a Fellow in Medicine, he completed his studies as a Research Fellow in the Research Division 1950-1952. He has been a Fellow in Medicine at the New York University College of Medicine, 1951-54.

He was certified by the American Board of Internal Medicine in 1954 and is an associate of the American Academy of Physicians. He is the associate Attending Internist at Hillside Hospital and has been directly responsible for the physiological studies of the Research Service, as well as coordinator of the biochemical programs.

3. Function of Research Service:

In addition to the research programs of the Research Service, the staff is active in two additional functions. They cooperate actively with those members of the hospital staff who are carrying on part-time research projects, chiefly of a clinical nature. In such instances, aid is given in the clarification of project goals, the planning and design of programs, and such technical assistance as is needed.

Secondly, an active resident training program is in progress, and during the third year, each resident is given an opportunity to carry on an independent project. Since the development of this service two projects have been completed, and three are now active. The completed projects include the clinical evaluation of reserpine in anxiety states and the use of testosterone as an adjuvant to insulin coma therapy. At present, resident projects include a study of the hospital milieu as a therapeutic factor, a clinical evaluation of chlorpromazine as a substitute for insulin coma therapy and clinical, psychologic and tachistoscopic measures of ambivalence.

In May, 1955, the Research Service established a liason with the Sloan-Kettering Institute of New York to carry out a cooperative study of steroid excretion rates in psychotic patients, with emphasis on the patterns altered during and following electroshock therapy.

VII. PRESENT BUDGET AND REQUESTED SUPPORT:

1. Present Budget and Present Support:

The following is the full budget of the Research Service for the fiscal year 1955-56. The major share of the program is supported by the Board of Directors, supplemented by grants of the United States Public Health Service. Under Grant M-927 of the National Institute of Mental Health, $14,807 of direct costs and $2221 of overhead costs was granted for the year September 1, 1955 to August 31, 1956. This grant is the second year of a 2-year grant for neurophysiological studies including the present Electroshock Evaluation Study. The National Institute of Arthritis has awarded $6500 for the second year of a two-year grant for biochemical studies.

		Board of Directors	U.S.P.H.S.
1. Personnel			
Director of Research	15,000	15,000	——
Psychiatry:			
Research Assistant in Psychiatry*	7,200	7,200	——
Research Assistant in Psychology	8,000	——	8,000
Research Assistant in Psychology	5,000	——	5,000
EEG Technician - Secretary	2,520	2,520	——
Biochemistry:			
Chief Chemist	8,600	8,600	——
Assistant Chemist	4,000	——	4,000
Assistant Chemist	2,800	2,800	——
Assistant in Chemistry	1,800	——	1,800
2. Equipment	450	——	450
3. Consumable Supplies	3,810	2,253	1,557
4. Travel - Conferences	1,200	1,000	200
Total	60,380	39,373	21,007
Overhead	2,521	——	2,521
TOTAL	62,901	39,373	23,528

* 3/5 time to September 1956.

2. Requested Budgetary Support:

A. The requirements of the Electroshock Therapy Evaluation Project include two additions to the professional staff, modification of two other positions, and specific allocations of equipment funds.

(1) Psychiatrist: The cooperation of an additional full time psychiatrist is needed to enlarge the scope of the study to include insulin coma therapy; to supervise the control study; to assist in the evaluations of change in patients and carry out follow-up studies. For this position, analytic experience is essential.

(2) Physiologist or Neurophysiologist: Present physiological studies are carried out by the Director and the Internist. Further study of physiological changes requires the coordination of these studies by a full-time physiologist, M.D. or Ph.D.

(3) Equipment: Present needs are focused in two areas - biochemistry and physiology. For further refined studies of the steroid sulfate patterns a recording attachment for the Beckman Spectrophotometer and a mechanical shaker (Dubnoff) are requested. To carry out the anticipated physiological studies modifications and attachments to the electroencephalograph are suggested.

B. The following budget is one suggested to continue the present program after July 1, 1956 with the addition of the personnel needed to complement the present staff. The budget is divided into three categories, following the three laboratory divisions which are coordinated in the Research Service. Estimates are listed for the first year, and for a five year period, including projected salary increments.

		First Year	Five Year Total
1. Psychiatry:			
a. Director	(20,-25,000)	20,000	112,500
Secretary	(2,6-3,100)	2,600	14,220
Conferences		1,200	6,000
b. Personnel			
1. Psychiatrist	(15,-18,000)	15,000	82,500
2. Psychiatrist	(15,-18,000)	15,000	82,500
3. Psychologist	(9,-12,000)	9,000	52,500
4. Psychologist	(5,5- 8,500)	5,500	35,000
c. Supplies & Equipment		1,200	3,600
Subtotal - Psychiatry		69,500	388,820
2. Neurophysiology:			
a. Personnel			
1. Physiologist	(9,-12,000)	9,000	52,500
2. Technician	(3,6-4,400)	3,600	12,000
b. Equipment		1,000	1,000
c. Supplies		1,200	6,000
Subtotal - Neurophysiology		14,800	71,500
3. Biochemistry:			
a. Personnel			
1. Chief Chemist	(9,-11,000)	9,000	51,000
2. Chemist	(6,-8,400)	6,000	36,000
3. Chemist	(4,-6,000)	4,000	25,000
4. Assistant	(1,8-2,600)	1,800	11,200
b. Equipment		7,000	7,000
c. Supplies		1,500	7,500
Subtotal - Biochemistry		29,300	137,700

	First Year	Five Year Total
Total -- All Programs	113,600	598,020
Overhead Allowance (15%)	17,040	89,700
TOTAL -- All Programs	130,640	687,720

C. Budget Reconciliation:

1. Salaries: The salary range for each item is consistent with present positions established at the hospital, or for new positions, with neighboring institutions. Present salary range for supervising psychiatrists is $12,-15,000, with a projected revision to the stated scale in 1956.

2. Equipment: For psychiatry, the initial year includes the equipment expenditure for tape recording system ($600) and an annual $600 allowance for expenses. The physiological equipment expense ($1000) is to allow modification of present electroencephalographic equipment to record other physiological indices. The expenditure for supplies includes allowances for consumable items and the provision for the building of specialized equipment. In biochemistry, the intiial expenditure includes $7,200 for a recording attachment for the Beckman spectrophotometer and $800 for a Dubnoff shaker.

3. Conferences: Present budgetary items include this sum for the use of the Director or members of the staff to attend appropriate scientific meetings.

4. Overhead: Consistent with hospital policy and recent administrative changes in other grants, a 15% allowance is requested. This amount includes hospital allocations for Social Security coverage; and for such contingencies in the expenses of the program as not requiring a significant alteration in the budget.

5. Subtotals and Total: The budget is presented in three sections, representing natural subdivisions of the program, thereby allowing for modifications in support.

VII. APPENDIX

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ANNUAL REPORT - DEPARTMENT OF NEUROLOGY

Studies of the alteration in perception with changes in brain function were the focus of activities of the Department of Neurology during the past year. A laboratory for electroencephalography was established, and newer methods for studying organic mental syndromes were introduced.

A group of related study projects were undertaken. The previous investigations of the response of subjects to simultaneous stimulation tests, begun by Dr. Bender, were continued with emphasis on the changes in perception in depressive illnesses, hysteria, and following electroconvulsive therapy. The effects of barbiturates, pervitin and lysergic acid (LSD-25) on such perceptual tests were intensively studied. In the latter part of the year, a correlated study of the changes in brain function during electroconvulsive therapy was undertaken. Two psychologists, Dr. Robert Kahn and Mr. H. Korin were appointed research assistants to the department, and Dr. Max Fink a fellow of the National Foundation for Infantile Paralysis was appointed to supervise the laboratory work.

On October 1, 1953 an electroencephalographic laboratory was established with a Medcraft 8 channel instrument. In the initial three months 65 records were taken. Of these 19 were consultation requests and 46 in the course of the integrated study on altered brain function.

During the year, 55 consultation requests were answered. More than half were for evaluations of organic mental states associated with depressive illness, or related to electroshock therapy. Seizure disorders, neuritic types of pain, and abnormal involuntary movements made up the bulk of remaining requests. Six patients with seizure disorders were followed and controlled with analeptic drugs. Three patients were transferred to the Neurological Service of Mt. Sinai Hospital for further investigations for neurological conditions observed at the hospital.

Two procedural changes were introduced by the department. As an aid to evaluating the organic mental states, the "amytal test"* was introduced and utilized. For the past half year, this test has found increasing use in following the course of electroshock treatments, and also as part of the integrated study on electroshock. In addition, the use of succinyl-choline chloride (anectine) as an adjuvant in electroshock replacing curare-like agents was demonstrated. This agent is more efficacious in inducing relaxation and has now supplanted other relaxing agents in indicated cases of electroshock at the hospital.

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