

**EXPERIMENTAL PSYCHIATRIC RESEARCH
AT HILLSIDE
Review and Prospect
MAX FINK, M.D.**

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The dedication of Hillside Hospital as a Research Institute has been a dream of many of its students—a dream that may achieve realization in this decade. Dr. Tarachow was an early proponent of this view; and both in his sponsorship of the Journal, and in his encouragement of research studies, he presaged this development. He was also the inadvertent sire of the research studies in experimental psychiatry. While I was a resident in psychiatry in 1952, we collaborated in a study of the relation of the early separation of child from a parent to the adult choice of neurosis. Reviewing the hospital records of five previous years we concluded that there was, indeed, a relation—neurotic patients with obsessional neuroses had a significantly greater incidence of separation than patients with hysterical neuroses (2). This report was the beginning of the patient population studies described here.

Since 1954 the various programs in experimental psychiatry have been devoted to an understanding of the mode of action of the psychiatric therapies of the hospital. The techniques have been adapted from descriptive and dynamic psychiatry, neuropsychology, electroencephalography, linguistics, pharmacology, and sociology. This report reviews these studies and presents support for the creation of a Research Institute at Hillside.

PAST STUDIES

In our early studies of convulsive therapy, instituted with the

¹ From the Department of Experimental Psychiatry, Hillside Hospital, Glen Oaks, N. Y.

The studies reported here have been aided by the Board of Directors Research Fund; the National Institute of Mental Health (Grants M-927; MY-2092,-2715,-4798; MF-12,033); Foundations Fund for Research in Psychiatry (FFRP 56-151); Kaufmann, and Dazian Foundations; and numerous pharmaceutical concerns including Geigy, Bristol, Wyeth and Smith, Kline & French Laboratories.

aid of a grant award of the National Institute of Mental Health, evaluations of patient improvement were shown to be dependent both on changes in brain function and on psychological factors. As our understanding of convulsive therapy developed, a general neurophysiologic-adaptive view of somatic therapies emerged (6).

A change in brain function was seen as a necessary condition for behavioral change, with the type of change varying, depending upon psychological and sociological characteristics of the subject (22, 25). Thus, the mode of action was not seen as either "organic" or "psychological" but rather as the interaction of neurophysiological changes and individual patterns of response and behavior.

This hypothesis was sustained in studies of convulsive and insulin coma therapies (21, 22); and the mode of action of the new psychotropic agents was expressed within this hypothesis. It was suggested that psychotropic drugs would be effective to the extent that persistent changes in brain function were induced; and that the type of behavioral response would be related to the type of brain change, and to individual premorbid psychologic (personality) patterns (6, 28, 40).

1. *Convulsive Therapy Process*: Seeking a measure of altered neurophysiological change that was sensitive and suitable for repeated retests, various measures were studied including changes in the face-hand test (1, 10, 13, 35), memory tests (17, 35), amount of slow-wave activity in the EEG (16, 23) and confabulatory and denial language patterns after amobarbital (3, 15). The latter two, EEG and amobarbital tests, were the most sensitive indices of change in convulsive therapy subjects. In one experiment, clinical ratings of improvement were correlated with high degrees of change in these indices (15, 16).

These observations were tested in a double-blind study in which patients referred for electroshock were randomly assigned to either convulsive or subconvulsive therapy. High degrees of electrographic slow-wave activity and positive amobarbital tests were observed only in the convulsive group; improvement rates were significantly higher in this group, and when subconvulsive subjects were retreated by convulsive applications, the improvement rate was similar to the convulsive group (22).

In subconvulsive applications, considerable electric current passes between the electrodes. It was postulated that the therapeutic agent was not the total electrical current per se, but the "all or none" quality manifested by the grand-mal seizure (9, 23, 42). The signifi-

cance of the grand-mal seizure was examined in a comparative study of the inhalant convulsant, hexafluorodiethylether (Indoklon), and electrically induced seizures. Similar degrees of electrographic change, improvement rates, types of behavioral adaptations, and changes in neuropsychological task behavior were observed in both the inhalant and in the electrically treated groups (49).

However, not all subjects manifesting high degrees of physiological change were evaluated as "improved." In a descriptive typologic study, five adaptive modes were described, empirically termed "euphoric," "hypomanic," "somatization," "paranoid-withdrawal," and "panic." While the first two patterns were rated as "much improved," the latter two were seen as "unimproved" or "worse" (50).

In studies of psychological variables, it was reported that patients rated "much improved" and "recovered" frequently manifested personality patterns akin to the explicit verbal denial personality type (37). These patients expressed the "language of denial" more frequently than unimproved subjects, exhibiting such aspects as explicit denial, minimization, displacement and clichés (27). Other psychological indices also related to favorable outcome included high F Scale score (42), Rorschach determinants of color, absent movement and absent form-color (30, 45), and low educational achievement and foreign birth (31).

2. *Anticholinergic Compounds and Convulsive Therapy*: Seeking a way to augment the degree of postconvulsive EEG slow-wave activity, an anticholinergic compound diethazine, was given intravenously at various stages of the convulsive therapy process (20, 24). Unexpectedly, diethazine caused an immediate and sustained decrease in EEG slowing, which was associated with marked changes in language and mood. In patients with denial language patterns (27), these could no longer be elicited. Instead of euphoria and well-being, the subjects became irritable, anxious, and complaining. In subjects prior to convulsive or drug therapy, diethazine induced excitement, tension, anxiety, and illusory sensations.

Subsequent studies with other central anticholinergic compounds and sympathomimetic hallucinogens showed behavior and electrographic patterns similar to diethazine. These observations led to the suggestion that an increase in the cholinergic activity of the central nervous system was the biochemical basis for the convulsive therapy process (38).

3. *Psychotropic Drugs and EEG*: Following these studies, the neurophysiological changes induced by drugs were tested within an

acute experimental EEG setting. It was observed that phenothiazines induced EEG synchronization and a shifting of the frequency spectrum to the slow frequencies; meprobamate and barbiturates, an increased synchronization and a shift of the spectrum to fast frequencies; reserpine, an increased slowing with synchronization at low dosages, and desynchronization at higher levels (18, 26, 28, 40). Imipramine induced desynchronization with a shift of frequencies to the slow bands (33, 34). Each active psychotropic compound was thus shown to have a characteristic frequency pattern.

Various other experimental compounds were also tested, and for these no consistent electrographic pattern was recorded. These compounds have since been shown to have either no or very limited clinical psychotropic activity. The absence of behavioral change with these compounds lent further support to the assumption that brain change is a necessary condition for the action of psychotropic drugs.

These observations suggested that psychopharmacological agents provide a means for eliciting various types of altered brain function in contrast to the single pattern following convulsive therapy. Furthermore, the type of neurophysiological alteration, as reflected in EEG synchrony and frequency patterns, was found to be related to specified types of behavioral adaptation. The advantage of EEG techniques for the assay of new psychotropic agents and the technical merits of electronic frequency analysis were assayed and described (47, 52).

4. *Insulin Coma Therapy*: In our insulin coma studies we confirmed earlier observations that persistent alterations of brain function were related to prolonged coma and spontaneous seizures; and saw in this relationship support for a neurophysiologic-adaptive hypothesis. With the availability of the new psychotropic agent chlorpromazine, a controlled chlorpromazine-insulin coma study was undertaken in September, 1955. As patients were referred for insulin coma they were randomly assigned to courses of either oral chlorpromazine for at least three months in doses adjusted to fall short of toxicity; or insulin coma, induced by a standard technique at least fifty times in each patient. While a number of minor differences were noted in comparing the two therapies, the results at time of discharge showed no statistical difference in the effectiveness of both treatments. Neither treatment seemed to affect the basic schizophrenic process, but chlorpromazine had the advantage of being safer, easier to administer, and better suited to long-term management (21). Concurrently, following the suggestion by the Creedmoor workers that

divided insulin doses were superior to single insulin doses, Blumberg and Laderman (39) essayed this problem and demonstrated no significant merit to the multiple-dose technique. (*In 1958, following the general confirmation of these observations, insulin coma therapy was discontinued at Hillside*).

5. *Neuropsychology*: Various psychophysical tests were adapted from neuropsychology, where their significance in brain-damaged subjects had been demonstrated. The early studies assessed these tasks as indices of altered brain function (35), and measured the range of performances of psychiatric patients, who are generally assumed not to be brain-damaged. Thus, memory function was assessed on immediate recall, after various interpolated learning tasks (17, 35), as well as during convulsive therapy (17). Tactile perceptual tasks were first examined in the clinical population (1). Later, with more sensitive electrical tactile stimuli, Korin (10) observed the range of thresholds in different body parts, the changes with altered brain function (10), and the influence of set (instruction) on performance (36). We also studied the perception of embedded geometric figures (43), tachistoscopic presentation of embedded color figures (55), perception of the visual upright (55), critical flicker frequency (49), and interference in reading time by delayed auditory feedback (55). For each task, the degree of decrement in task performance was found to be positively correlated with the amount of EEG slowing. Following treatment completion, with the return of physiological indices to pretreatment levels, performance in these psychological tasks also returned to pretreatment levels, or higher—a betterment of performance ascribed to practice effect.

Concurrently, assessment of various psychological measures as indices predictive of behavioral change during convulsive and drug therapies led to studies of the Rorschach determinants (30, 45), California F Scale scores (30, 42), language patterns after amobarbital (27), denial scores on interview (37), and the perception of the visual upright and auditory feedback (55).

6. *Psycholinguistics*: Concurrent with the syntactic language studies (27), analyses of other language patterns were undertaken, both in a search for more objective indices of behavioral change and to gain experience in the technical problems of tape analysis for psychotherapy research. An index of variability in the vocabulary of speech, the type-token ratio (TTR) of consecutive samples of dyadic speech, was extensively studied (7, 41, 44, 46, 56, 57).

In convulsive therapy patients, significant changes in TTR mean

and standard deviations were related both to the degree of induced EEG slow-wave activity and to syntactic language patterns obtained in independent structured interviews. It was noted that speech became more repetitive (lowered mean TTR) and more variable in consecutive samples (41). In interviews before and after the intravenous administration of centrally active agents, similar changes were observed. Agents which produced predominant synchronization patterns on the EEG were related to a decrease in mean TTR and an increase in the standard deviation of scores, while desynchronizing compounds elicited greater variability in speech patterns and decrease in variability of consecutive scores (44).

Other language measures studied included distress-relief quotients, self-reference, and alterations in tense and person. It was suggested that these psycholinguistic measures are useful techniques for the operational analyses of physiological and psychological effects of psychopharmacological agents (44, 46).

7. *Brain Damage and Schizophrenia*: Following his studies at Ittleson Center, Pollack reviewed the relationship between age of hospitalization, intellectual functioning and prognosis in schizophrenic children and adults. He noted that initial hospitalization in childhood and adolescence was related to I. Q. scores in the subnormal range, deviant performance on psychomotor tasks, and more frequent ratings of "unimproved" at hospital discharge than was initial hospitalization as an adult. The early and insidious onset of the behavioral syndrome "schizophrenia" was thus related to brain dysfunction (54). Findings suggest that different subgroups of schizophrenia may be classified on the basis of neuropsychological deviancy.

8. *Sociological Studies*: Considerable interest in the family organization to which discharged patients were returning, the relation of social factors to choice and results of psychiatric treatment, and the specific problem of the relation of these factors to treatment referral patterns led to a series of population studies. In one study (8), education, age, place of birth, and score on the California F Scale were significantly related to the type of therapy received and the utilization of adjunctive hospital services. In a second study (31), duration of hospitalization, discharge evaluation, and diagnosis were related to the same social factors, while in a study of patient refusal of ECT, similar relationships were observed (51).

These observations suggested a comparative interinstitution study, and among three hospitals the relationships between social class and other demographic variables (age, sex, education) to the clinical

variables of patient classification (diagnosis), duration of hospitalization, selection of therapy, and discharge evaluation have been assessed. Three teaching institutions were selected in which all therapies are equally available to all patients—Menninger Foundation Hospital (upper-class, Protestant), Massachusetts Mental Health Center (lower-class, Catholic), and Hillside Hospital (middle-class, Jewish). In such a comparison we have found the differences in designations of treatment, diagnosis, and discharge evaluation so marked as to make comparisons difficult. While many relationships between social variables and clinical variables were observed in each hospital, no social variable was found related to the clinical variables in every hospital (53).

In an outpatient department study, sex, age, and marital status were found to be related to the acceptance and rejection of patients and failure to complete the application process (55).

These observations in population samples led to concurrent studies of staff attitudes in the selection of therapy (11, 12). In a series of ward observation studies, Kaplan and Lefkowitz indicated the significant role of staff attitudes (especially nursing personnel) in the referral for subjects for somatic therapies, and in the transfer of patients from one ward to another. (*To study the influence of staff attitude on patient selection for drug therapy, we requested one ward be designated as a "no-movement" unit. This was adopted in September, 1959 and shortly thereafter by the whole hospital.*)

PRESENT STUDIES

During the period of the convulsive therapy studies, many new psychotropic compounds were assessed clinically (5, 21), electrographically (34, 40, 48), and psychophysically (48). The present psychopharmacology evaluation program, based on these studies, was designed to answer the following questions:

1. Is there a relation between measurable alteration in brain function and behavioral change with psychotropic drugs on chronic administration?
2. Are there pretreatment clusters of psychiatric, physiological, and psychological variables which are related to the type of behavioral adaptation?
3. Are such clusters related to the type and degree of physiological change?

As an initial approximation, a double-blind, fixed dosage, ran-

dom assignment drug study was undertaken. Based on our clinical experiences three types of compounds were selected on the basis of their EEG patterns. In this study, 203 subjects were referred, and 149 have completed the testing program, from October, 1959 to July, 1961.

1. *Behavioral Change*: In a survey of the behavioral adaptations of patients receiving various psychotropic compounds during 1958-59, a behavioral typology based on the treatment response and on pretreatment psychiatric profiles was developed (55). In the present study, the typologies are being tested, and various measures of behavioral change studied, including therapist ratings, self-ratings, and various ward observation scales.

2. *Neuropsychology*: Psychological tasks have been viewed both as indices of behavioral change and as predictive guides in convulsive therapy. Each of these tasks and a selected group of motor tasks are now being assessed for both their capacity to reveal change with various drugs and their capacity to predict change with the drugs in this program (48).

3. *Electroencephalography*: In the convulsive therapy studies, the degree of EEG slowing was measured by counting the consecutive waves in selected samples (16). When the more subtle changes of drug effects are studied, it is necessary to apply less tedious techniques (48), and electronic frequency analysis was introduced in August, 1959. By measurement of the pen deflection for various frequencies from 3 to 33 cps in ten-second epochs, rapid measurement of apparently small changes in total activity and frequency spectra are obtained (52).

Other physiological variables studied in this program include the response of EEG to intravenous chlorpromazine, blood pressure response to mecholyl, the EKG, radioactive iodine uptake, and analyses of various blood and urine elements.

4. *Data Analysis*: To analyze the data generated in this study, we have sought the aid of complex statistical methods and computational facilities. Analyses of covariance, correlation matrices, factor analyses, and discriminant function analyses are computations now in progress with these data at the NIMH Psychopharmacology Service Center's Biometric Laboratory in Washington.

THE NEXT STEPS

Favored by a national research climate and a cooperative hospital staff, these studies have proceeded vigorously. The assets for research in this setting have been great—a selected, intelligent patient popula-

tion resident from six to twelve months, without individual economic limitation of hospital stay; a sophisticated administration tolerant of controlled studies; and approval of a Board of Directors who desire "research" as an institutional function.

As Dr. Lewis Robbins noted in his first hospital report in 1959, a specialty hospital can make little impact on the mental illness problems of the community by treatment alone. The successful treatment of 350 patients a year is but little comfort to the 40,000 resident patients in the state hospitals of Long Island. Nor will the annual training of twenty or thirty physicians in the arts of psychotherapy do much to help these unfortunates or the many thousands of ambulatory mentally ill resident in the nation. No, a therapeutic goal alone is salutary but inadequate to our needs. As he proposed, the answer may lie in the dedication of a "research hospital," as it is here that a specialty hospital can truly excel.

The charter has been written in the Board's assertion of research as a hospital goal. With the assets of an exemplary therapeutic facility, such rededication can provide the stimulus for the continuous study of the cause of mental illness and of methods of therapy.

Such dedication would provide the stimulus for comparative and controlled assessments of different therapeutic techniques. Continued study is urgently required of the selection of patients for various therapies; the application and mode of action of the therapies; and the role of social and milieu factors in supporting the effects of our therapies.

Assessments require a meaningful classification of subjects. The behavioral variables alone, which are the basis of our present diagnostic schemata, are unsatisfactory. Study is urgently required of the applicability of social and demographic variables; psychological task performance profiles; typologies based on behavioral response to defined stresses or drugs; and physiological reactivity measures. Such classifications are also essential for any biochemical, physiological, or evaluative study to provide homogeneous samples and comparable controls.

Assessments also require meaningful indices of evaluating change. Present global "improvement" ratings and socialization measures are inadequate. Whether the intervening variable be milieu therapy, psychotherapy, drug therapy, or time, the criteria of behavioral change require definition. The applicability of rating scales, language tasks, self-ratings, psychophysical change scores, family assessments, etc., require study and evaluation.

Recent studies of psychotic subjects have provided the suggestion

that there is a neurologic factor in a group of the schizophrenias. The high incidence of electrographic and neurologic dysfunction, the lack of behavioral response to all therapies, and the relentless course of the illness suggest an "organic" involvement in this cluster. Such a substrate must be clearly sought by the application of biochemical, neurophysiological, and epidemiological techniques to various clusters of young psychotic subjects.

These are broader views of some of the questions studied in the programs in experimental psychiatry of the past seven years. These programs, and the contemporary projects in biochemistry and in medicine, provide models of bootstrap studies undertaken with limited support. A dedication of Hillside Hospital as a Research Institute will provide the needed focus and impetus for the scientific and humanitarian forces of the community to join in a common endeavor to resolve the problems of the mentally ill.

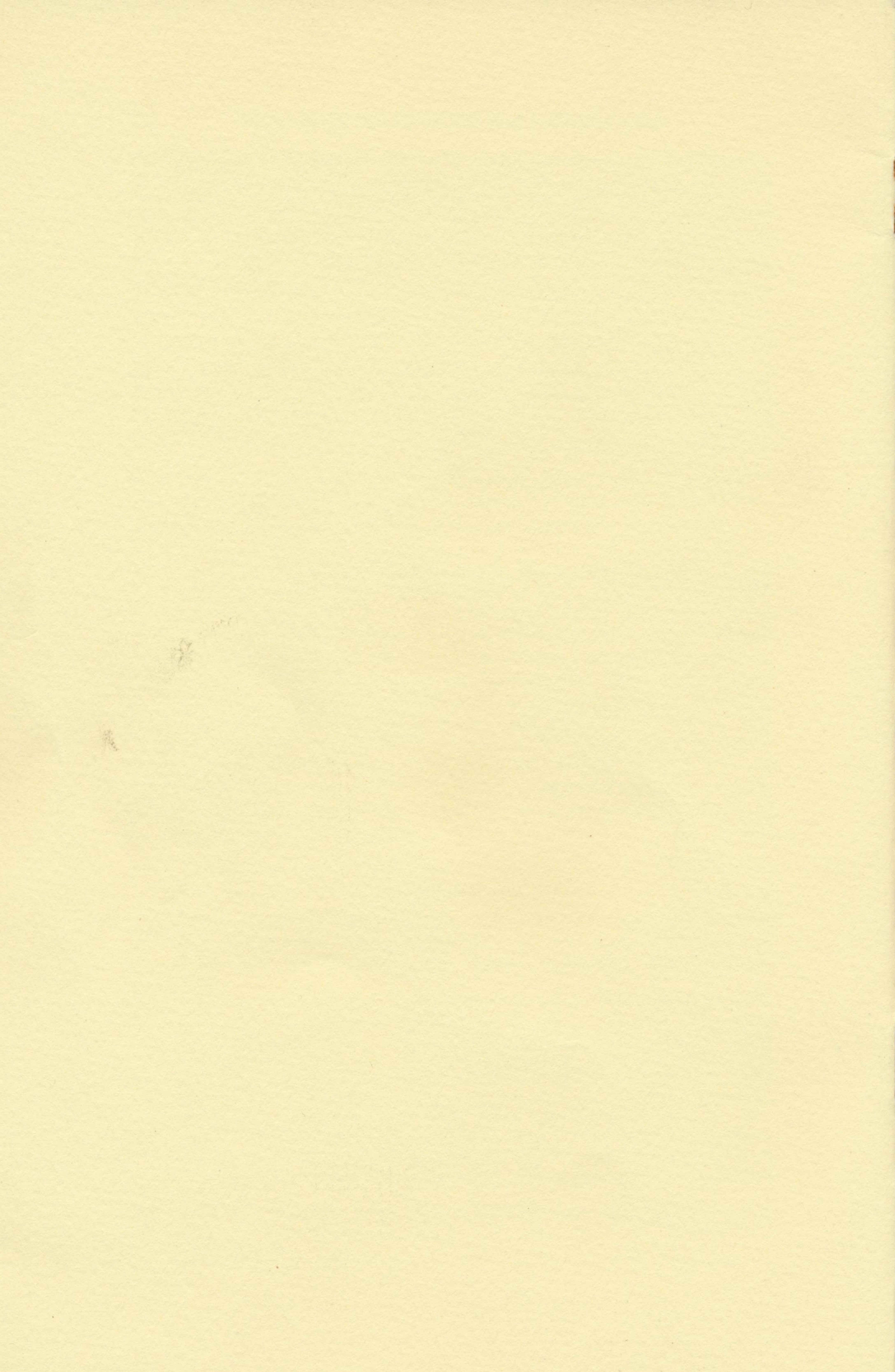
Acknowledgment: Participants in these programs include the present members of the Department of Experimental Psychiatry: Ira Belmont, Martin A. Green, Abraham Kaplan, Eric Karp, Donald F. Klein, John C. Kramer, Max Pollack, and Arthur Willner. Former associates included Karl Andermann, Joseph Jaffe, Robert L. Kahn, Hyman Korin, George Krauthamer, Nathaniel Siegel; and Research Fellows Barre Alan, Fred Coleman, Harold Esecover, Stanley Friedman, Henry J. Lefkowitz, and Robert Shaw. The cooperation of Arnold G. Blumberg of the Department of Medicine in the present program is gratefully acknowledged. The reports listed here are the result of the collaboration of these workers and the professional staffs of the hospital who gave unstintingly of their time and their good-will.

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* Due to the length of this Bibliography, it is presented in an abbreviated form.



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doses were superior to single insulin doses, Blumberg and Laderman essayed this problem and demonstrated no significant merit to the multiple dose technique (29). (In 1958, following the general confirmation of these observations, insulin coma therapy was discontinued at Hillside).

5. Neuropsychology: Various psychophysical tests were adapted from neuropsychology, where their significance in brain damaged subjects had been demonstrated. The early studies assessed these tasks as indices of altered brain function (35), and measured the range of performances of psychiatric patients, who are generally assumed not to be brain damaged. Thus, memory function was assessed on immediate recall, after various interpolated learning tasks (17,35), as well as during convulsive therapy (17). Tactile perceptual tasks were first examined in the clinical population (1). Later, with more sensitive electrical tactile stimuli, Korin observed the range of thresholds in different body parts (10), the changes with altered brain function (10) and the influence of set (instruction) on performance (36). We also studied the perception of embedded geometric figures (43), tachistoscopic presentation of embedded color figures (55), perception of the visual upright (55), critical flicker frequency (49) and interference in reading time by delayed auditory feedback (55). For each task, the degree of decrement in task performance

was found to be positively correlated with the amount of EEG slowing. Following treatment completion, with the return of physiological indices to pre-treatment levels, performance in these psychological tasks also returned to pre-treatment levels, or higher - a betterment of performance ascribed to practice effect.

Concurrently, assessment of various psychological measures as indices predictive of behavioral change during convulsive and drug therapies led to studies of the Rorschach determinants (30,45), California F Scale scores (30,42), language patterns after amobarbital (27), denial scores on interview (37) and the perception of the visual upright and auditory feedback (55).

6. Psycholinguistics: Concurrent with the syntactic language studies (27), analyses of other language patterns were undertaken, both in a search for more objective indices of behavioral change and to gain experience in the technical problems of tape analysis for psychotherapy research. An index of variability in the vocabulary of speech, the type-token-ratio (TTR) of consecutive samples of dyadic speech, was extensively studied (7,41,44,46,56).

In convulsive therapy patients, significant changes in TTR mean and standard deviations were related both to the degree of induced EEG slow wave activity and to syntactic

language patterns obtained in independent structured interviews. It was noted that speech became more repetitive (lowered mean TTR) and more variable in consecutive samples (41). In interviews before and after the intravenous administration of centrally active agents, similar changes were observed. Agents which produced predominant synchronization patterns on the EEG were related to a decrease in mean TTR and an increase in the standard deviation of scores, while desynchronizing compounds elicited greater variability in speech patterns and decrease in variability of consecutive scores (44).

Other language measures studied included distress-relief quotients, self-reference, and alterations in tense and person. It was suggested that these psycholinguistic measures are useful techniques for the operational analyses of physiological and psychological effects of psychopharmacological agents (44,46).

7. Brain Damage and Schizophrenia: Following his studies at Ittleson Center, Pollack reviewed the relationship between age of hospitalization, intellectual functioning and prognosis in schizophrenic children and adults. He noted that initial hospitalization in childhood and adolescence was related to I.Q. scores in the subnormal range, deviant performance on psychomotor tasks, and more

frequent ratings of "unimproved" at hospital discharge than was initial hospitalization as an adult. The early and insidious onset of the behavioral syndrome "schizophrenia" was thus related to brain dysfunction (57). Findings suggest that different subgroups of schizophrenia may be classified on the basis of neuropsychological deviancy.

8. Sociological Studies: Considerable interest in the family organization to which discharged patients were returning, the relation of social factors to choice and results of psychiatric treatment, and the specific problem of the relation of these factors to treatment referral patterns led to a series of population studies. In one study (8), education, age, place of birth and score on the California F scale were significantly related to the type of therapy received and the utilization of adjunctive hospital services. In a second study (31), duration of hospitalization, discharge evaluation and diagnosis were related to the same social factors, while in a study of patient refusal of ECT, similar relationships were observed (51).

These observations suggested a comparative inter-institution study, and among three hospitals the relationships between social class and other demographic variables (age, sex, education) to the clinical variables

of patient classification (diagnosis), duration of hospitalization, selection of therapy and discharge evaluation have been assessed. Three teaching institutions were selected in which all therapies are equally available to all patients, - Menninger Foundation Hospital (upper-class, Protestant), Massachusetts Mental Health Center (lower-class, Catholic) and Hillside Hospital (middle-class, Jewish). In such a comparison we have found the differences in designations of treatment, diagnosis and discharge evaluation so different as to make comparisons difficult. While many relationships between social variables and clinical variables were observed in each hospital, no social variable was found related to the clinical variables in every hospital (53).

In an Out-Patient Department study, sex, age and marital status were found to be related to the acceptance and rejection of patients and failure to complete the application process (54).

These observations in population samples led to concurrent studies of staff attitudes in the selection of therapy (11,12). In a series of ward observation studies, Kaplan and Lefkowitz indicated the significant role of staff attitudes (especially nursing personnel) in the referral for subjects for somatic therapies, and in the transfer of patients from one ward to another. (To study

the influence of staff attitude on patient selection for drug therapy, we requested one ward be designated as a "no-movement" unit. This was adapted in September 1959 and shortly thereafter by the whole hospital.)

PRESENT STUDIES

During the period of the convulsive therapy studies, many new psychotropic compounds were assessed clinically (5,21) electrographically (34,40,48) and psychophysically (48). The present psychopharmacology evaluation program, based on these studies, was designed to answer the following questions:

Is there a relation between measurable alteration in brain function and behavioral change with psychotropic drugs on chronic administration?

Are there pre-treatment clusters of psychiatric, physiological and psychological variables which are related to the type of behavioral adaptation?

Are such clusters related to the type and degree of physiological change?

As an initial approximation, a double-blind, fixed dosage, random assignment drug study was undertaken. Based on our clinical experiences three types of compounds were

selected on the basis of their EEG patterns. In this study, 203 subjects were referred and 149 have completed the testing program, from October 1959 to July 1961.

1. Behavioral Change: In a survey of the behavioral adaptations of patients receiving various psychotropic compounds during 1958-59, a behavioral typology based on the treatment response and on pre-treatment psychiatric profiles was developed (55). In the present study, the typologies are being tested, and various measures of behavioral change studied, including therapist ratings, self-ratings and various ward observation scales.

2. Neuropsychology: Psychological tasks have been viewed both as indices of behavioral change and as predictive guides in convulsive therapy. Each of these tasks and a selected group of motor tasks are now being assessed for both their capacity to reveal change with various drugs and their capacity to predict change with the drugs in this program (48).

3. Electroencephalography: In the convulsive therapy studies, the degree of EEG slowing was measured by counting the consecutive waves in selected samples (16). When the more subtle changes of drug effects are studied, it is necessary to apply less tedious techniques (48), and electronic frequency analysis was introduced in August, 1959. By measurement of the pen deflection for various

frequencies from 3 to 33 cps in ten second epochs, rapid measurement of apparently small changes in total activity and frequency spectra are obtained.(52).

Other physiological variables studied in this program include the response of EEG to intravenous chlorpromazine, blood pressure response to mecholyl, the EKG, radioactive iodine uptake, and analyses of various blood and urine elements.

4. Data Analysis: To analyze the data generated in this study, we have sought the aid of complex statistical methods and computational facilities. Analyses of covariance, correlation matrices, factor analyses and discriminant function analyses are computations now in progress with this data at the NIMH Psychopharmacology Service Center's Biometric Laboratory in Washington.

THE NEXT STEPS

Favored by a national research climate and a cooperative hospital staff, these studies have proceeded vigorously. The assets for research in this setting have been great -- a selected, intelligent patient population resident from six to twelve months, without individual economic limitation of hospital stay; a sophisticated administration tolerant of controlled studies; and approval of a Board of Directors who desire "research" as an institutional function.

As Dr. Lewis Robbins noted in his first hospital report in 1959, a specialty hospital can make little impact on the mental illness problems of the community by treatment alone. The successful treatment of 350 patients a year is but little comfort to the 40,000 resident patients in the state hospitals of Long Island. Nor will the annual training of twenty or thirty physicians in the arts of psychotherapy do much to help these unfortunates or the many thousands of ambulatory mentally ill resident in the nation. No, a therapeutic goal alone is salutary but inadequate to our needs. As he proposed, the answer may lie in the dedication of a "research hospital", as it is here that a specialty hospital can truly excel.

The charter has been written in the Board's assertion of research as a hospital goal. With the assets of an exemplary therapeutic facility, such rededication can provide the stimulus for the continuous study of the causes of mental illness and of methods of therapy.

Such dedication would provide the stimulus for comparative and controlled assessments of different therapeutic techniques. Continued study is urgently required of the selection of patients for various therapies; the application and mode of action of the therapies; and the role of social and milieu factors in supporting the effects

of our therapies.

Assessments require a meaningful classification of subjects. The behavioral variables alone, which are the basis of our present diagnostic schemata, are unsatisfactory. Study is urgently required of the applicability of social and demographic variables; psychological task performance profiles; typologies based on behavioral response to defined stresses or drugs; and physiological reactivity measures. Such classifications are also essential for any biochemical, physiological or evaluative study to provide homogenous samples and comparable controls.

Assessments also require meaningful indices of evaluating change. Present global "improvement" ratings and socialization measures are inadequate. Whether the intervening variable be milieu therapy, psychotherapy, drug therapy or time, the criteria of behavioral change require definition. The applicability of rating scales, language tasks, self-ratings, psychophysical change scores, family assessments, etc. require study and evaluation.

Recent studies of psychotic subjects has provided the suggestion that there is a neurologic factor in a group of the schizophrenias. The high incidence of electrographic and neurologic dysfunction, the lack of behavioral response to all therapies, and the relentless course of

the illness suggests an "organic" involvement in this cluster. Such a substrate must be clearly sought by the application of biochemical, neurophysiological and epidemiological techniques to various clusters of young psychotic subjects.

These are broader views of some of the questions studied in the programs in experimental psychiatry of the past seven years. These programs, and the contemporary projects in biochemistry and in medicine, provide models of boot-strap studies undertaken with limited support. A dedication of Hillside Hospital as a Research Institute will provide the needed focus and impetus for the scientific and humanitarian forces of the community to join in a common endeavor to resolve the problems of the mentally ill.

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