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Experimental Psychiatric Programs at Hillside Hospital

A Review

The various programs in the Department of Experimental Psychiatry have been devoted to an understanding of the mode of action of ~~various~~ psychiatric therapies ~~in psychiatry~~ through studies of brain function. The principal techniques have been adapted from descriptive psychiatry, neuropsychology, electroencephalography, linguistics, pharmacology, and sociology.

In initial studies of convulsive therapy, changes in brain function were found to relate both to improvement ratings and to pre-treatment psychologic variables. As our understanding of convulsive therapy developed, a general neurophysiologic-adaptive view of somatic therapies emerged ( ). In this view psychiatric treatments are seen as therapeutically affective to the degree that brain function in measurably altered. While change in brain function is necessary for behavioral change, the type of adaptation, however, varies depending upon pre-treatment psychological and sociological characteristics of the subject. Thus, the mode of action is not seen as either "organic" or "psychologic" but rather as the interaction of both aspects in the individual. Further, while behavioral change is

related to changes in brain function, and the adaptive pattern to pre-treatment psychological characteristics, evaluations of 'improvement', being special types of evaluation of change, are derivative judgments based on staff and family expectations and tolerances.

This hypothesis was developed and sustained in a series of studies of convulsive therapy. Concurrent studies of insulin coma indicated that behavioral change here, too, was related to the onset and degree of prolonged coma or repeated seizures - these being the principal manifestations of prolonged neurophysiological change in this therapy.

The mode of action of the new psychotropic agents was also expressed within this hypothesis ( ). It was suggested that these agents would be effective to the degree that they induced persistent changes in brain function' and that the type of behavioral response would be related to the type of brain change, and to premorbid psychological (personality) patterns. The present programs in the Department are designed to study these relationships in detail.

Convulsive Therapy Process

Of various measures of brain function, the amount of slow wave activity in the electroencephalogram and confabulatory and

denial language patterns after amobarbital ( ) were the most sensitive indices in convulsive therapy subjects. In the first experiment, improvement ratings were found to be correlated directly with the appearance of high degrees of change in these indices ( ). These observations were tested in a double-blind study in which patients referred for electroshock were randomly assigned to courses of either convulsive or subconvulsive therapy under pentothal premedication. High degrees of neurophysiologic change were observed only in the convulsive group; improvement rates were significantly higher in this group; and when subconvulsive subjects were re-treated by convulsive applications, the improvement rate was similar to the original convulsive group.

In the subconvulsive treated subjects, considerable amounts of electrical current passed between the bitemporal electrodes. It was concluded, therefore, that the therapeutic agent was not the total electrical current, <u>per se</u>, but an all or none quality manifested by the grand mal seizure. The significance of the grand mal seizure was further elaborated in studies of the inhalant convulsant, hexafluorodiethylether (Indoklon). Similar degrees of electrographic change, improvement rates, types of behavioral

change and changes in neuropsychologic task behavior were observed in the inhalant and in electrically treated groups.

It was soon apparent, however, that not all subjects manifesting high degrees of physiologic change were rated as 'improved'. In a descriptive typologic study, five patterns were described, emperically termed 'euphoric', 'hypomanic', 'somatization', 'paranoid-withdrawal', and 'panic'. While the first two of these adaptive modes were rated as 'much improved', the latter two were seen as 'unimproved' or 'worse' ( ).

In studies of psychologic variables, it was reported that patients rated as 'much improved' and 'recovered' frequently manifested personality patterns similar to that described by Weinstein and Kahn ( ) as the explicit verbal denial personality. In language patterns, they expressed the language of denial, when diffuse brain change was induced, exhibiting such aspects as denial, minimization, displacement, cliches, etc. more frequently than unimproved subjects. Other indices related to favorable outcome were high F Scale score ( ), and Rorschach determinants of color, absent movement and absent form-color ( ). In this population, also, favorable outcome was associated with low educational achievement

and foreign birth ( ).

Anticholinergics and Convulsive Therapy

Seeking a way to augment the degree of post-convulsive EEG slow wave activity, an anticholinergic compound, diethazine, was given intravenously at various stages of the convulsive therapy process. Contrary to expectations, diethazine caused an immediate and sustained decrease in EEG slowing. Patients with denial language patterns relingquished them. Instead of euphoria and well being, the subjects were irritable, anxious and expressive of pre-treatment patterns. In subjects prior to convulsive or drug therapy, diethazine induced excitement, tension, anxiety and illusory sensations.

Subsequent studies with other central anticholinergic compounds (WIN-2299, JB-318,336, benactyzine) showed behavioral and electrographic patterns simmlar to diethazine. Similar desynchronization of post-convulsive EEG slowing was also noted with central sympathomimetic hallucinogens (amphetamine, mescaline, LSD-25), and has been reported for antihistamines (dephenlydramine). These observations led to the suggestion that an increase in central cholinergic activity was a biochemical basis for the convulsive

therapy process ( ).

Psychotropic Drugs and EEG

During this period,the mode of action of newer psychotropic drugs aroused interest. Following the concepts derived from convulsive therapy, the neurophysiologic changes induced by drugs were tested within the same experimental setting of acute experiments in an EEG setting. It was observed that phenothiazines (chlorpromazine, promazine, trifluopromazine) induced EEG synchronization and a shifting of the spectrum to the slow frequencies; meprobamate and barbiturates , an increased synchronization and a shift of spectrum to fast frequencies; reserpine, an increased slowing with synchronization at low dosages, and desynchronization at higher levels. Imipramine induced desynchronization with a shift of frequencies to the slow bands.

Other experimental compounds tested included BL-M188 and phenyltoloxamine (Bristol), Deaner and its various congeners (Riker), WY-2149 (Wyeth) and frenquel (Merrill). For each, no consistent electrographic patterns emerged.

It was suggested that psychopharmacologic agents provide a means for eliciting a variety of neurophysiologic patterns in

contrast to the single pattern of induced convulsions. Furthermore, the type of neurophysiologic alteration, as reflected in EEG synchrony and frequency patterns, was related to specific types of behavioral adaptation. Increasing EEG synchrony and a shift to slow frequencies are associated with tranquillization, sedation and decreasing agitation; while desynchronization and a shift to fast frequencies is associated with excitement, illusions, and delusional ideation. These observations areconsistent with hypotheses of Wikler ( ). The merit of such techniques for the assay of new psychotropic agents has been described ( ).

Psychopharmacology Evaluation Program

The present program, instituted in October 1959, is based on these studies and is 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, physiologic and psychologic variables related to the type of behavioral adamptation? - to the type and degree of physiologic change?

Method: As an initial approximation, a double-blind, fixed dosage random assignment drug study was undertaken. Based on clinical experiences with various psychotropic compounds, three classes were selected on the basis of their patterns of EEG response. The selected agents were those with predominant desynchronizing patterns; synchronizing and slowing; or minimal or no effect. Patients referred for drug therapy, after medical examination, and after all other medications have been discontinued are randomly assigned to one of three classes of compounds.

Patients are predominantly middle class, urban, with high educational attainment. Hillside Hospital is a non-profit, philanthropic supported psychiatric institution, admitting voluntary

patients for extensive psychotherapeutic treatment. Mean duration of stay is seven months. Convulsive and psychotropic drug therapies are prescribed by staff psychiatrists on referral to the Department. All treatment is administered by Departmental staff, so that the experimental variables of drug dosage, route of administration, assignment to groups, etc. are readily controlled. All patients in the hospital are available for study.

After a testing period, all patients receive 40 cc of liquid medication daily from individually labelled bottles. Dosages are increased in fixed weekly steps until a maximum at 4 weeks. After two weeks on maximum dosage, re-testing occurs.

To date, 140 subjects have been referred, and 110 have completed the study period. Preliminary analyses of the data are now in progress.

Behavioral Change

In a survey of the behavioral adaptations of patients receiving phenothiazines or imipramine, various clusters of behaviors were developed. The typology was based on the treatment response and the pre-treatment psychiatric profile. In the present study, various measures of behavioral change are under study. Therapist referral questionnaires and six week evaluations; therapist and

patient Clyde Mood Scales; Lorr Scale evaluations in interview by two research psychiatrist, and Lorr Ward Scales; patient self-ratings including the Johns Hopkins symptom check list and the Chicago Attitude Scales are amongst the measures being explored.

Neuropsychology: Psychologic tasks are viewed both as change variables and predictive variables. In convulsive therapy, changes in memory tasks ( ), tactile perception ( ), Wechsler-Bellevue ( ), CFF ( ), Figure ground tasks ( ) , and tachistoscopic recognition of figures ( ) have been related to the degree of induced neuro-physiologic change. For each task, the degree of decrement in task performance has been positively correlated with the amount of EEG slowing. Following treatment completion, with the return of physiologic indices to pre-treatment levels, performance in these psychologic tasks also returns to pre-treatment levels, or higher - a betterment of performance ascribed to practice effect. Denial scores on interview ( ), Rorschack determinants ( ), F Scale scores ( ), auditory feedback ( ), language patterns after amobarbital ( ),and perception of the visual upright ( ) have been viewed as predictive indices of the behavioral changes following ECT. These various tasks are now being assessed with psychotropic agents.

Electroencephalography: In the convulsive therapy studies, the degree of EEG slowing was measured by counting the consecutive waves in selected samples. When the more subtle changes of drug effects were studied, it was necessary to apply less tedious techniques. 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 now obtained and applied.

Other physiologic variables include the response of EEG to intravenous chlorpromazine; blood pressure response to mecholyl; EKG; radioactive iodine uptake, and analyses of various blood and urine element ordinarily conceived as protective of the patient's welfare.

Psycholinguistics:

Following the studies of syntactic language patterns ( ) in convulsive therapy, other aspects of language were studied for their relation as indices of change in intrapersonal behavior. Jaffe, after considerable exploration with many linguistic measures, suggested that type-token-ratio (TTR) of consecutive samples of dyadic speech may be a useful index. While TTR had previously been applied to written texts or the langaage samples of individuals, Jaffe indicated that the two person communication (dyad) was a more significant index of the state of the interaction than analyses of separate samples of the participants.

Applying this technique to convulsive therapy patients, changes in TTR mean and standard deviation were related both to the degree of induced EEG slow wave activity and to syntactic language patterns obtained in independent structured interviews. Speech became more repetitive (lowered mean TTR) and more variable in consecutive samples (increased standard deviation) ( ).

In interviews before and after the intravenous administration of centrally active agents, similar changes were observed. Agents with a predominant synchronization pattern on the EEG exhibited a decrease in mean TTR and increase in standard deviation of scores,while desynchronizing compounds elicited greater variability in speech patterns (increase in TTR mean) and decrease in variability of consecutive scores (decrease in standard deviation).

Other language measures under study include distress-relief quotients, self-reference, and alteration in tense and person. It is suggested that these psycholinguistic measures are potent techniques for the operational analyses of physiologic and psychologic effects of psychopharmacologic agents ( ).

Sociologic Studies

The general problem of the relation of social factors to choice and results of psychiatric treatment, and the specific problem of the relation of these factors to the referral patterns, within the institution, led to a series of population studies. In one study ( ), 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. Thus, patients who were older, poorly educated had higher F scores and were foreign-born, particularly Eastern Europe, were most likely to be referred for electro-shock. These relationships were presently independent of diagnoses. Within the group of electroshock patients, time for referral for ECT was also related to these factors.

In a second study of this group ( ), duration of hospitalization, discharge evaluation and diagnoses were related to the same social factors. For example, patients hospitalized for the shortest period were oldest, had the least education, were most likely to have been foreign born and had the high F scale scores. Younger, native-born, more

educated, lower F scale score patients were hospitalized the longest. These relationships held true within treatment type and within diagnostic class. On discharge, older patients had the most favorable ratings. In ECT, patients rated as recovered or much improved had the highest F scores, least education and were most likely to be foreign born.

In a study of patient refusal of ECT, similar relationships were observed ( ). These relationships are now under study in the out-patient department, and in a tri-hospital comparative study. In the latter study, the populations of three hospitals in which all therapies are equally available to all patients, - Menninger Foundation Hospital (upper-class, Protestant), Massachusetts Mental Health C nter (lower-class Catholic) and Hillside Hospital (middle-class Jewish) are being assessed. It has been postulated that these relationships reflect the influence of social background on psychological processes, such as habitual patterns of communication and modes of expression. The contribution of these factors to the pattern of mental illness, and the patient-therapist interaction are under study.

Experimental Psychiatric Programs at Hillside Hospital:

A Review

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In initial studies of convulsive therapy, changes in brain function were found to relate both to evaluations of improvement and to pre-treatment psychologic variables. As our understanding of convulsive therapy developed, a general neurophysiologic-adaptive view of somatic therapies emerged (1). In this view psychiatric treatments are therapeutically effective to the degree that brain function is measurably altered. While change in brain function is necessary for behavioral change, the type of adaptation, however, varies depending upon pre-treatment psychologic and sociologic characteristics of the subject (2). Thus, the mode of action is not seen as either "organic" or "psychologic" but rather as the interaction of diffuse neurophysiologic changes and adaptive mechanisms. Further, while behavioral change is related to changes in brain function, and the adaptive pattern to pre-treatment psychologic characteristics, evaluations of 'improvement', being special types of evaluation of change, are derivative judgments based on staff and family expectations and tolerances (2).

This hypothesis was developed and sustained in a series of studies of convulsive therapy. Concurrent studies of insulin coma indicated that behavioral change here, too, was related to the onset and degree of prolonged coma or repeated seizures - these being the principal manifestations of prolonged neurophysiologic change in this therapy (3,4).

The mode of action of the new psychotropic agents was also expressed within this hypothesis (5,6). It was suggested that these agents would be effective to the degree that they induced persistent changes in brain function and that the type of behavioral response would be related to the type of brain change, and to premorbid psychologic (personality) patterns. The present programs in the Department are designed to study these relationships in detail.

CONVULSIVE THERAPY PROCESS

Of various measures of brain function, the amount of slow wave activity in the electroencephalogram (7,8) and confabulatory and denial language patterns after amobarbital (9,10) were the most sensitive indices (11) in convulsive therapy subjects. In one experiment, improvement ratings were correlated with the appearance of high degrees of change in these indices (7,10).

These observations were tested in a double-blind study in which patients referred for electroshock were randomly assigned to courses of either convulsive or subconvulsive therapy under pentothal premedication. High degrees of neurophysiologic change were observed only in the convulsive group; improvement rates were significantly higher in this group ; and when subconvulsive subjects

were re-treated by convulsive applications, the improvement rate was similar to the original convulsive group (2).

In the subconvulsive treated subjects, considerable amounts of electric current passed between the bitemporal electrodes. It appeared that the therapeutic agent was not the total electrical current, per se, but an all or none quality manifested by the grand mal seizure (8,12). The significance of the grand mal seizure was examined in studies of the inhalant convulsant, hexafluorodiethylether (Indoklon). Similar degrees of electrographic change, improvement rates, types of behavioral change and changes in neuropsychologic task behavior were observed in the inhalant and in electrically treated groups (13).

It was soon apparent that not all subjects manifesting high degrees of physiologic change were rated as 'improved'. In a descriptive typologic study, five patterns were described, empirically termed 'euphoric', 'hypomanic', 'somatization', 'paranoid-withdrawal', and 'panic'. While the first two of these adaptive modes were rated as 'much improved', the latter two were seen as 'unimproved' or 'worse' (14).

In studies of psychologic variables, it was reported that patients rated as 'much improved' and 'recovered' frequently manifested personality patterns similar to that described by Weinstein and Kahn as the explicit verbal denial personality. In language patterns, patients expressed the 'language of denial', when diffuse brain change was induced, exhibiting such aspects as explicit denial, minimization, displacement, cliches, etc. more frequently than unimproved subjects. Other indices related to favorable

outcome were high F Scale score (15), and Rorschach determinants of color, absent movement and absent form-color (16,17). In this population, also, favorable outcome was associated with low educational achievement and foreign birth (18).

ANTICHOLINERGIC COMPOUNDS AND CONVULSIVE THERAPY

Seeking a way to augment the degree of post-convulsive EEG slow wave activity, an anticholinergic compound, diethazine, was given intravenously at various stages of the convulsive therapy process (19). Contrary to expectations, diethazine caused an immediate and sustained decrease in EEG slowing. Patients with denial language patterns relinquished them. Instead of euphoria and well being, the subjects were irritable, anxious and expressive of pre-treatment patterns. In subjects prior to convulsive or drug therapy, diethazine induced excitement, tension, anxiety and illusory sensations.

Subsequeht studies with other central anticholinergic compounds (WIN-2299, JB-318,336, benactyzine) showed behavioral and electrographic patterns similar to diethazine. Similar desynchronization of post-convulsive EEG slowing was also noted with central sympathomimetic hallucinogens (amphetamine, mescaline, LSD-25), and has been reported for antihistamines (diphenylhydramine). These observations led to the suggestion that an increase in central cholinergic activity was a biochemical basis for the convulsive therapy process (20).

PSYCHOTROPIC DRUGS AND EEG

During this period, the mode of action of newer psychotropic drugs aroused interest. Following the concepts derived from convulsive therapy, the neurophysiologic changes induced by drugs

were tested within the same acute experimental framework of the EEG setting. It was observed that phenothiazines (chlorpromazine, promazine, trifluopromazine) induced EEG synchronization and a shifting of the spectrum to the slow frequencies; meprobanate and barbiturates, an increased synchronization and a shift of spectrum to fast frequencies; reserpine, an increased slowing with synchronization at low dosages, and desynchronization at higher levels (5,6). Imipramine induced desynchronization with a shift of frequencies to the slow bands (21).

Other experimental compounds tested included BL-MI88 and phenyltoloxamine (Bristol), Deaner and its various congeners (Riker), WY-2149 (Wyeth) and frenquel (Merrill). For each, no consistent electrographic pattern was recorded.

It was suggested that psychopharmacologic agents provide a means for eliciting a variety of neurophysiologic patterns in contrast to the single pattern of induced convulsions. Furthermore, the type of neurophysiologic alteration, as reflected in EEG synchrony and frequency patterns, was related to specified types of behavioral adaptation. Increasing EEG synchrony and a shift to slow frequencies were associated with tranquillization, sedation and decreasing agitation; while desynchronization and a shift to fast frequencies was associated with excitement, illusions, and delusional ideation (6,20). These observations are consistent with hypotheses of Wikler. The advantages of EEG techniques for the assay of new psychotropic agents have already been reported (6).

PSYCHOPHARMACOLOGY EVALUATION PROGRAM

The present program, instituted in October 1959, is based on these studies and is 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, physiologic and psychologic variables related to the type of behavioral adaptation?

And, are such clusters related to the type and degree of physiologic change?

Method: As an initial approximation, a double-blind, fixed dosage random assignment drug study was undertaken. Based on our clinical experiences with various psychotropic compounds from 1954 to 1959, three classes were selected on the basis of their patterns of EEG response. The agents selected were those with either predominant desynchronizing patterns, synchronizing and slowing, or minimal or no effect. Patients referred for drug therapy, after medical examination, and after all other medications have been discontinued are randomly assigned to a compound in one of these three classes.

Patients are predominantly middle class, urban, with high educational attainment. Hillside Hospital is a non-profit, philanthropic supported psychiatric institution, admitting voluntary patients for extensive psychotherapeutic treatment. The mean duration of stay for patients is seven months. Convulsive and psychotropic drug therapies are prescribed by staff psychiatrists

on referral to the Department. All treatment is administered by Departmental staff, so that the experimental variables of drug dosage, route of administration, assignment to groups, etc. are readily controlled. All patients in the hospital are available for study.

After a testing period, all patients receive 40 cc of liquid medication daily from individually labelled bottles. Dosages are increased in fixed weekly steps until a maximum at 4 weeks. After two weeks on maximum dosage, re-testing occurs.

To date, 140 subjects have been referred, and 110 have completed the study period. Preliminary analyses of the data are now in progress.

Behavioral Change: In a survey of the behavioral adaptations of patients receiving phenothiazines or imipramine during 1958-59, various clusters of behaviors were developed. The typologies were based on the treatment response and on pre-treatment psychiatric profiles. In the present study, the typologies are being tested, and various measures of behavioral change are being studied. These include therapist referral questionnaires and six week evaluations; therapist and patient Clyde Mood Scales; Lorr Scale evaluations in interview by two research psychiatrists, and Lorr Ward Scales; and patient self-ratings including the Johns Hopkins symptom check list and the Chicago Attitude Scales.

Neuropsychology: Psychologic tasks have been viewed both as change variables and predictive variables. In convulsive therapy, changes in memory tasks (22), tactile perception (23,24), Wechsler-Bellevue (13), CFF (13), figure-ground tasks (25), and tachistoscopic recognition of figures (26) were related to the degree of induced

neurophysiologic change. 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 physiologic indices to pre-treatment levels, performance in these psychologic tasks also returned to pre-treatment levels, or higher - a betterment of performance ascribed to practice effect.

Denial scores on interview (27), Rorschach determinants (16,17), F S F Scale scores (15,17), language patterns after amobarbital (28), auditory feedback and perception of the visual upright have been viewed as predictive indices of the behavioral changes following ECT.

These various tasks are now being assessed with psychotropic agents, for their capacity to change with various agents, or their capacity to predict change.

Electroencephalography: In the convulsive therapy studies, the degree of EEG slowing was measured by counting the consecutive waves in selected samples (7). When the more subtle changes of drug effects are studied, it is necessary to apply less tedious techniques. 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 now obtained and applied.

Other physiologic 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.

PSYCHOLINGUISTICS

Another series of studies in the Department have been devoted to formal language patterns.

Following the studies of syntactic language patterns (28) in convulsive therapy, other aspects of language were studied for their relation as indices of change in interpersonal behavior. Jaffe, after considerable exploration with various linguistic measures, suggested that type-token-ratios (TTR) of consecutive samples of dyadic speech may be a useful index (29,30). While TTR had previously been applied to written texts or the language samples of individuals, Jaffe indicated that the two person communication (dyad) was a more significant index of the state of the interaction than analyses of separate samples of the participants.

Applying this technique to convulsive therapy patients, changes in TTR mean and atandard deviations were related both to the degree of induced EEG slow wave activity and to syntactic language patterns obtained in independent structured interviews. Speech became more repetitive (lowered mean TTR) and more variable in consecutive samples (increased standard deviation) (31). In interviews before and after the intravenous administration of centrally active agents, similar changes were observed. Agents with a predominant synchronization pattern on the EEG exhibited a decrease in mean TTR and increase in standard deviation of scores, while desynchronizing compounds elicited greater variability in speech patterns (increase in TTR mean) and decrease in variability of consecutive scores (decrease in standard deviation) (32).

Other language measures studied included distress-relief quotients, self-reference, and alteration in tense and person.

It was suggested that these psycholinguistic measures are potent techniques for the operational analyses of physiologic and psychologic effects of psychopharmacologic agents (32).

SOCIOLOGIC STUDIES

In the course of these psychiatric programs, considerable interest was engendered in the family organization to which patients were returning. Also, the general problem of the relation of social factors to choice and results of psychiatric treatment, and the specific problem of the relation of these factors to the referral patterns led to a series of population studies. In one study (33), 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. Thus, patients who were older, poorly educated, had higher F scores and were foreign-born, particularly Eastern Europe, were most likely to be referred for electroshock. These relationships were present independent of diagnoses. Within the group of electroshock patients, the time for referral for ECT was also related to these factors.

In a second study (18), duration of hospitalization, discharge evaluation and diagnoses were related to the same social factors. For example, patients hospitalized for the shortest period were oldest, had the least education, were most likely to have been foreign-born and had the higher F Scale scores. Younger, native-born, more educated, lower F Scale score patients were hospitalized the longest. These relationships held true within treatment type and within diagnostic class. On discharge, older patients had the most favorable ratings. In ECT, patients rated as recovered or much improved had the highest F scores, least education and were most likely to be foreign-born. In another study of patient refusal of ECT, similar relationships were observed (34).

These relationships are now under study in the Out-Patient Department, and in a tri-hospital comparative study. In the latter study, the populations of three hospitals with prevailing differing clients, 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) are being assessed. It has been postulated that these relationships reflect the influence of social background on psychological processes, such as habitual patterns of communication and modes of expression. The contribution of these factors to the pattern of mental illness, and the patient-therapist interaction are under study.

SUMMARY

The Departmental programs are a cluster of interrelated studies focussed about common population samples. Within Hillside Hospital, research laboratories in Biochemistry, and in Medicine are active; and other laboratories in psychodynamic psychiatry are being developed. In this Department, various disciplines are participants,representing a gradual growth of six years. Further growth and the directions of ensuing studies are dependent on the results of the studies described here; as well as the growing institutional awareness that research is an integral part of the hospital's operation and budgets - as much as treatment and staff training.

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These observations were tested in a double-blind study in which patients referred for electroshock were randomly assigned to courses of either convulsive or subconvulsive therapy under pentothal premedication. High degrees of neurophysiological change were observed only in the convulsive group; improvement rates were significantly higher in this group; and when subconvulsive subjects

were re-treated by convulsive applications, the improvement rate was similar to the original convulsive group (2).

In the subconvulsive treated subjects, considerable amounts of electric current passed between the bitemporal electrodes. It appeared that the therapeutic agent was not the total electrical current, per se, but an all or none quality manifested by the grand mal seizure (8,12). The significance of the grand mal seizure was examined in studies of the inhalant convulsant, hexafluorodiethylether (Indoklon). Similar degrees of electrographic change, improvement rates, types of behavioral change and changes in neuropsychologic/al task behavior were observed in the inhalant and in electrically treated groups (13).

It was soon apparent that not all subjects manifesting high degrees of physiologic change were rated as 'improved'. In a descriptive typologic study, five patterns were described, empirically termed 'euphoric', 'hypomanic', 'somatization', 'paranoid-withdrawal', and 'panic'. While the first two of these adaptive modes were rated as 'much improved', the latter two were seen as 'unimproved' or 'worse' (14).

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outcome were high F Scale score (15), and Rorschach determinants of color, absent movement and absent form-color (16,17). In this population, also, favorable outcome was associated with low educational achievement and foreign birth (18).

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Seeking a way to augment the degree of post-convulsive EEG slow wave activity, an anticholinergic compound, diethazine, was given intravenously at various stages of the convulsive therapy process (19). Contrary to expectations, diethazine caused an immediate and sustained decrease in EEG slowing. Patients with denial language patterns relinquished them. Instead of euphoria and well being, the subjects were irritable, anxious and expressive of pre-treatment patterns. In subjects prior to convulsive or drug therapy, diethazine induced excitement, tension, anxiety and illusory sensations.

Subsequent studies with other central anticholinergic compounds (WIN-2299, JB-318,336, benactyzine) showed behavioral and electrographic patterns similar to diethazine. Similar desynchronization of post-convulsive EEG slowing was also noted with central sympathomimetic hallucinogens (amphetamine, mescaline, LSD-25), and has been reported for antihistamines (diphenylhydramine). These observations led to the suggestion that an increase in central cholinergic activity was a biochemical basis for the convulsive therapy process (20).

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And, are such clusters related to the type and degree of physiologic change?#

Method: As an initial approximation, a double-blind, fixed dosage random assignment drug study was undertaken. Based on our clinical experiences with various psychotropic compounds from 1954 to 1959, three classes were selected on the basis of their patterns of EEG response. The agents selected were those with either predominant desynchronizing patterns, synchronizing and slowing, or minimal or no effect. Patients referred for drug therapy, after medical examination, and after all other medications have been discontinued are randomly assigned to a compound in one of these three classes.

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Following the studies of syntactic language patterns (28) in convulsive therapy, other aspects of language were studied for their relation as indices of change in interpersonal behavior. Jaffe, after considerable exploration with various linguistic measures, suggested that type-token-ratios (TTR) of consecutive samples of dyadic speech may be a useful index (29,30). While TTR had previously been applied to written texts or the language samples of individuals, Jaffe indicated that the two person communication (dyad) was a more significant index of the state of the interaction than analyses of separate samples of the participants.

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Other language measures studied included distress-relief quotients, self-reference, and alteration in tense and person.

It was suggested that these psycholinguistic measures are potent techniques for the operational analyses of physiological and psychological effects of psychopharmacologic agents (32).

SOCIOLOGIC STUDIES

In the course of these psychiatric programs, considerable interest was engendered in the family organization to which patients were returning. Also, the general problem of the relation of social factors to choice and results of psychiatric treatment, and the specific problem of the relation of these factors to the referral patterns led to a series of population studies. In one study (33), 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. Thus, patients who were older, poorly educated, had higher F scores and were foreign-born, particularly in Eastern Europe, were most likely to be referred for electroshock. These relationships were present independent of diagnoses. Within the group of electroshock patients, the time for referral for ECT was also related to these factors.

In a second study (18), duration of hospitalization, discharge evaluation and diagnoses were related to the same social factors. For example, patients hospitalized for the shortest period were oldest, had the least education, were most likely to have been foreign-born and had the higher F Scale scores. Younger, native-born, more educated, lower F Scale score patients were hospitalized the longest. These relationships held true within treatment type and within diagnostic class. On discharge, older patients had the most favorable ratings. In ECT, patients rated as recovered or much improved had the highest F scores, least education and were most likely to be foreign-born. In another study of patient refusal of ECT, similar relationships were observed (34).

These relationships are now under study in the Out-Patient Department, and in a tri-hospital comparative study. In the latter study, the populations of three hospitals with prevailing differing clients, 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) are being assessed. It has been postulated that these relationships reflect the influence of social background on psychological processes, such as habitual patterns of communication and modes of expression. The contribution of these factors to the pattern of mental illness, and the patient-therapist interaction are under study.

SUMMARY

The Departmental programs are a cluster of interrelated studies focussed about common population samples. Within Hillside Hospital, research laboratories in Biochemistry, and in Medicine are active; and other laboratories in psychodynamic psychiatry are being developed. In this Department, various disciplines are participants,representing a gradual growth of six years. Further growth and the directions of ensuing studies are dependent on the results of the studies described here; as well as the growing institutional awareness that research is an integral part of the hospital's operation and budgets - as much as treatment and staff training.

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Experimental Psychiatric Programs at Hillside Hospital: A Review

Max Fink, M.D.

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

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Experimental Psychiatric Programs at Hillside Hospital

A Review

The various programs in the Department of Experimental Psychiatry have been devoted to an understanding of the mode of action of psychiatric therapies through studies of brain function. The principal techniques have been adapted from descriptive psychiatry, neuropsychology, electroencephalography, linguistics, pharmacology, and sociology.

In initial studies of convulsive therapy, changes in brain function were found to relate both to evaluations of improvement and to pre-treatment psychological variables. As our understanding of convulsive therapy developed, a general neurophysiologic-adaptive view of somatic therapies emerged (1). In this view psychiatric treatments are seen as therapeutically effective to the degree that brain function is measurably altered. While change in brain function is necessary for behavioral change, the type of adaptation, however, varies depending upon pre-treatment psychological and sociological characteristics of the subject (2). Thus, the mode of action is not seen as either "organic" or "psychologic" but rather as the interaction of diffuse neurophysiologic changes and adaptive mechanisms. Further, while behavioral change is related to changes in brain function, and the adaptive pattern to pre-treatment psychologic characteristics, evaluations of 'improvement', being special types of evaluation of change, are derivative judgements based on staff and family expectations and tolerances (2).

This hypothesis was developed and sustained in a series of studies of convulsive therapy. Concurrent studies of insulin coma indicated that behavioral change here, too, was related to the onset and degree of prolonged coma or repeated seizures - these being the principal manifestations of prolonged neurophysiological change in this therapy (3,4).

The mode of action of the new psychotropic agents was also expressed within this hypothesis (5,6). It was suggested that these agents would be effective to the degree that they induced persistent changes in brain function and that the type of behavioral response would be related to the type of brain change, and to premorbid psychologic (personality) patterns. The present programs in the Department are designed to study these relationships in detail.

CONVULSIVE THERAPY PROCESS

Of various measures of brain function, the amount of slow wave activity in the electroencephalogram (7,8) and confabulatory and denial language patterns after amobarbital (9,10) were the most sensitive indices (11) in convulsive therapy subjects. In one experiment, improvement ratings were correlated with the appearance of high degrees of change in these indices (7,10).

These observations were tested in a double-blind study in which patients referred for electroshock were randomly assigned to courses of either convulsive or subconvulsive therapy under pentothal premedication. High degrees of neurophysiological change were observed only in the convulsive group; improvement rates were

significantly higher in this group; and when subconvulsive subjects were re-treated by convulsive applications, the improvement rate was similar to the original convulsive group (2).

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Review and Prospect

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Review and Prospect

MAX FINK, M.D.

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

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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 Lefkowits 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 iittle 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.

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