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Final Report

ALTERED BRAIN FUNCTION FOLLOWING ELECTROSHOCK

(Perceptual Changes Induced by Drugs and Electroshock)

From the

Department of Experimental Psychiatry

Hillside Hospital

Glen Oaks, L.I., N.Y.

September 1, 1959

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FINAL REPORT

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HILLSIDE HOSPITAL
Glen Oaks, L. I., N. Y.

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Altered Brain Function Following Electroshock

Progress Report #4 February 1, 1958 - September 1, 1959

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ALTERED BRAIN FUNCTION FOLLOWING ELECTROSHOCK

SUMMARY:

In the past eighteen months, the various studies of the convulsive therapy process were completed and extended, and an investigation of psychopharmacologic agents begun. The framework for these investigations has been the neurophysiologic-adaptive view of convulsive therapy (Weinstein and Kahn, 1955; Fink and Kahn, 1957) extended to insulin coma and drug therapies in psychiatry (Fink, 1957).

The following aspects of the convulsive therapy process were studied:

1. Significance of the Convulsion: A comparative study of the neurophysiologic, psychologic and behavioral effects of electrical and inhalant (Indoklon) induced convulsions.

2. Synaptic Basis of Neurophysiologic Change: Further studies of the effects of acute administration of experimental anticholinergic and sympathomimetic agents on both the "normal" and post-convulsive EEG.

3. Sociopsychologic Aspects of Convulsive Therapy:

a. Relation of the factors of age, education, nativity and stereotypy (measured by the California F Scale) to the selection of therapy, duration of hospitalization, diagnosis and discharge ratings.

b. Changes of F score with treatment, and relation of these changes to EEG indices.

4. Psychotherapy and Convulsive Therapy: In supervisory sessions, alterations in the psychotherapeutic relationship with convulsive therapy were observed.

5. Perception: Both patterns of change and individual differences on tachistoscopic figure-ground discrimination tasks and perception of the upright with induced convulsions.

These studies were extended to drug therapies and the following studies undertaken:

1. Neurophysiologic:

a. Relation of EEG change on acute and chronic administration of various psychopharmaceuticals to clinical behavioral change.

b. EEG as a screening device for psychopharmacologic potency.

c. Relation of EEG changes to hallucinogenic activity.

d. EEG effects of megimide.

2. Communication Patterns: Relation of induced neurophysiologic change to dyadic diversification and syntactic language measures.

3. Sociopsychologic Studies: Aspects of the doctor-patient relationship affecting choice of somatic therapy.

These studies have supported and expanded the neurophysiologic-adaptive view of convulsive therapy, and demonstrated that such a hypothesis has applicability to our understanding of the mode of action of psychopharmacologic agents.

PROGRESS REPORT

A. THE CONVULSIVE THERAPY PROCESS.

1. Significance of the Convulsion:

An earlier convulsive-subconvulsive control study had demonstrated that significant behavioral changes occurred almost exclusively in patients receiving grand mal convulsive therapy. The present report is an assessment of the neurophysiologic, behavioral and clinical effects of two different methods of inducing convulsions - electrical and inhalent.

Twenty-five consecutive patients referred for convulsive therapy were randomly classified into two groups with seizures induced in thirteen patients by the standard Medcraft alternating current instrument, and in twelve by the inhalation of hexafluorodiethyl-ether (Indoklon). In both groups treatment was administered three times a week for a total of 10 to 24 applications, determined by clinical criteria by the supervising psychiatrist.

All patients were tested one to two days prior to the first treatment, following the 10-12th treatment, and two weeks following the last treatment. In addition to evaluations of behavioral change, tests included measures of intellectual function (five subtests from the Wechsler-Bellevue Intelligence Scale), perception (figure-ground discrimination using embedded geometric figures, the perception of pseudoisochromatic color plates at high speeds of tachistoscopic exposure, and the Street incomplete figures test), and social attitude (the Levinson revision of the California F Scale). An electro-

encephalogram was obtained during each of the testing periods, and measured for the per cent time slow wave (6 cps or slower) activity from a continuous 66 second sample.

The results failed to show any significant intergroup test differences between the electroshock and Indoklon groups at each of the three test periods.

Intragroup analysis, however, showed that during treatment both groups made increased errors on the intellectual and perceptual tests, and had higher scores on the F scale. By two weeks after the termination of treatment both groups returned to near pretreatment levels for most tests.

Both groups were comparable for the degree of induced EEG slow wave activity after 10-12 treatments. The per cent time slow wave activity for the Indoklon group was 51% and for the electroshock group 47.5%. Within each group individual differences in behavioral change were related to the degree of neurophysiologic change - those with the highest degree of EEG change showing the greatest behavioral change. Rank order correlations between changes in test performance and the degree of slow wave activity with treatment were positive for all procedures, except the comprehension subtest of the Wechsler-Bellevue, and reached a level of statistical significance for digit span (+ .61, $p < .01$), object assembly (+ .46, $p < .05$), F scale (+ .38, $p < .05$), tachistoscopic perception (+ .67, $p < .01$) and perception of embedded figures (+ .43, $p < .05$).

Two different convulsant agents thus produced similar neurophysiologic and perceptual behavioral changes; and it was concluded that the behavioral change in convulsive therapy is related to the degree of altered brain function, and is non-specific for the type of agent used to induce the convulsion.

(Presented, in part, at the Eastern Psychological Association, Atlantic City, April, 1959).

2. Biochemical Aspects of the Convulsive Therapy Process:

The significance of high voltage EEG slow wave activity in the convulsive therapy process (Roth et al, 1951, 1957; Fink and Kahn, 1957) and the report that this activity was blocked by the administration of such anticholinergic agents as atropine and scopolamine (Ulett and Johnson, 1957) provided the basis for these studies. As there were attendant unpleasant systemic effects with the administration of these agents, reports describing diethazine as an anticholinergic compound with potent neurologic but minimal systemic effects (Jenkner and Lechner, 1955; Lechner, 1956) led to studies similar to those of Ulett and Johnson using this compound (Fink, 1958). These observations with diethazine further led to the investigation of other experimental anticholinergic agents.

Clinical and electroencephalographic responses to the intravenous administration of diethazine, Win-2299, benactyzine, JB-318, JB-336 and atropine in psychiatric patients at various

stages of convulsive therapy were studied. Each is a potent anticholinergic agent in vitro.

The subjects were ninety psychiatric patients referred for convulsive therapy, ranging in age from 18 to 67, with a variety of diagnoses. A total of 107 observations were made, as some subjects were studied with more than one compound.

The observations were made in the EEG laboratory using a standard 8 channel instrument and needle electrodes. In each trial, the compound under study was administered intravenously at a set rate per minute until clinical behavioral or electrographic changes were observed.

It was observed that administration of these anticholinergic agents was associated with a) desynchronization of EEG rhythms with a blocking of post-convulsive delta activity; b) alerting, excitatory behavioral response with illusory, delusional and hallucinatory ideation, and c) systemic effects of muscular weakness, dryness of the mouth, dry skin and tachycardia. The electrographic, behavioral and systemic effects were concurrent.

These observations are regarded as consistent with the suggestion that the physiologic basis of convulsive therapy lies in an increase in central nervous system cholinergic activity.

Observations that LSD, amphetamine, mescaline and diphenhydramine - sympathomimetic and antihistaminic agents - also induced EEG desynchronization, blocking of post convulsive delta

activity and clinical excitatory activity support the suggestion that the behavioral and electrographic patterns of these compounds are also based on an alteration in synaptic activity. Increased synaptic activity (cholinergic, sympatholytic effects) is associated with EEG hypersynchronization, and clinical sedation and euphoria; while decreased synaptic activity (anticholinergic, sympathomimetic) is associated with EEG desynchronization and clinical excitatory and hallucinogenic states, thus supporting a hypothesis initially described by Wikler (1954). It was also suggested in these studies that the discrepant observations of EEG slow wave activity after the administration of atropine was related to significant differences in dosage and to species specificity.

(Presented, in part, at the Society of Biological Psychiatry, San Francisco, 1958 and awarded the first A.E. Bennett Psychiatric Research Award of that Society; and, in part, at American EEG Society, Atlantic City, 1958. Published, in part, A.M.A. Arch. Neurol. & Psychiat. 80: 380-387, 1957; and accepted for publication, EEG Clin. Neurophysiol.)

3. Sociopsychologic Aspects of Psychiatric Treatment:

a. Duration of Hospitalization, Diagnosis and Discharge Evaluation.

In an earlier study of the Hillside Hospital population (Kahn, Pollack and Fink, 1957), it was noted that age, education, place of birth and social attitudes as measured by the California F scale, were related to the selection of therapy. Those patients who were older, had less education, were foreign-born and with high stereotypy scores on the F Scale

were more likely to receive convulsive therapy. In contrast, patients who were younger, better educated, native-born and who obtained low scores on the F Scale, received psychotherapy as their sole form of treatment.

This study was extended to determine the relations of these sociopsychologic factors to 1) the duration of hospitalization, 2) the clinical evaluations at time of discharge, and 3) the final diagnosis.

The entire in-patient adult population on March 7, 1957 was studied. This consisted of 171 patients, 57 men and 114 women, ranging in age from 16 to 68 years, with a median of 35 years.

Patients hospitalized for the shortest period (1-5 months) were noted to be the oldest, have the least education, were most likely to be foreign-born, and have the highest scores on the F Scale. Younger, native-born, more educated, lower F score patients were hospitalized the longest (10 or more months). The same relationship of these factors to length of hospitalization was found when separate analyses were made according to diagnosis and type of treatment (convulsive therapy or psychotherapy).

Discharge evaluations of improvement were significantly related to age - the older patients having the most favorable ratings. Analysis of the data by type of treatment, however, demonstrated that among the convulsive therapy patients ratings of recovered or much improved were given to those patients with

the highest F scores, least education and who were foreign-born.

Diagnoses of schizophrenia or psychoneurosis were associated with lower F scores, younger ages, more education and native birth. The older, less educated, foreign-born, high F score patients were more frequently classified as involutional or manic-depressive psychosis.

It was postulated that these relationships reflect the influence of social background and psychological processes, such as the behavioral patterns of communication and mode of expression; and that these relationships contribute not only to the pattern of mental illness, but affect all aspects of the patient-therapist interaction.

(Presented at the Eastern Psychological Association, Atlantic City, and the Academy of Psychoanalysis, Philadelphia, April, 1959. Accepted for publication, Archives of General Psychiatry.)

b. Changes in Social Attitude with Convulsive Treatment.

Following earlier observations that the California F Scale is useful in understanding the reason for referral for convulsive therapy and the evaluation of clinical response following such treatment, further studies were undertaken with this scale in regard to the following questions: 1) What does the F Scale measure in a psychiatric population? 2) Do F scores change with convulsive therapy? 3) Are these changes related to the degree of altered brain function?

The entire in-patient population of the hospital was given the F Scale, and one month later, was retested with a "reverse" F Scale, in which each statement was changed to the opposite of the original. The "reverse" scale was scored in the same manner as the conventional scale, with high scores reflecting greater agreement.

It was noted that those patients who made low scores initially, indicating a predominant disagreement with the statements, showed an increase on the "reverse" scale, indicating a high degree of agreement. In contrast, patients who made high scores initially showed little change on retesting, agreeing with the statements to the same extent even though the meaning was reversed. It is evident that low F score patients are more critical and discriminating persons, while those with high F scores are more undifferentiating and stereotyped in their reactions.

This observation is related to the process of selection of patients for convulsive therapy. A high degree of stereotypy of thinking and communication is incompatible with the establishment of a conventional psychotherapeutic relationship, thus inhibiting the psychoanalytically-oriented psychotherapy stressed at this hospital. It follows that the high F score patients will be unsuccessful in psychotherapy and most likely referred for convulsive therapy.

In another study, sixty-nine patients were given the F Scale before, during (at 10-12 treatment period) and after

convulsive therapy. Ten patients, selected at random, constituted a control group and received subconvulsive electrostimulation. There was a mean increase in F score of +5.7 during treatment in the convulsive group - a difference significant at the 5% level. In contrast, the control group showed an insignificant change during the same period (+0.5). The extent of increase in the convulsive patients was related to the degree of cerebral dysfunction as determined by slow wave activity on the EEG. The patients with high delta (more than 40% of the sample record) had a mean increase of +8.6. Those patients with low delta indices, however, showed an increase of +3.4. Following treatment the F scores were comparable to the pretreatment levels.

These findings support and elaborate previous observations on the effects of convulsive therapy. Greater agreement with the F Scale statements during treatment show conventional stereotypy and difficulty in discrimination. Changes in F score thus parallel the characteristic language changes of increased denial, evasion, qualification, and use of cliches and stereotyped expressions (Kahn and Fink, 1958). It is also comparable to the increased difficulty in complex visual and tactile perception (Fink, Kahn and Korin, 1957) and figure-ground discrimination (Kahn and Fink, 1957).

(Presented at the Eastern Psychological Association, 1958; and accepted for presentation at the Divisional Meeting of the American Psychiatric Association, New York, November 1959).

4. Psychotherapy and Physiodynamic Therapy:

Previous studies indicated that patients referred for electroshock in this hospital are of two types. The larger group are patients of an older age who have limited education and are foreign born. They tend to be non-introspective persons, stereotyped in their language and thinking, and verbally uncommunicative. Symptoms of depression, agitation, withdrawal and somatization are prominent. The second, and smaller, group of patients are younger, native-born, better-educated, and verbally communicative with a capacity for introspection. They characteristically exhibit thinking disorders and overactive behavior, with lesser degrees of somatization and depression.

Four patients, two from each group described above were studied to determine 1) reasons for referral, 2) whether different attitudes were required in psychotherapeutic management, and 3) the relation of the psychotherapeutic approach to the patient's clinical response to convulsive therapy.

It was concluded that these patients were referred for convulsive therapy because of difficulty in communication in the psychotherapeutic relationship. In two cases this was a reflection of the patient's limited verbal and introspective capacity related to educational and social factors. In two instances, however, the impaired communication was reflected in acting-out behavior.

Following treatment, the older, less educated patients were able to sustain the behavioral change with a reassuring, supportive technique, amplifying tendencies to minimization and denial developed during electroshock. In the better educated patients, the decreased acting-out behavior was associated with increased interpretive psychotherapy.

It was suggested that the relationship of psychotherapy to convulsive therapy various with the communication pattern and adaptation shown by the individual patient.

Published in the Journal of Hillside Hospital, 7: 17-25, 1958).

5. Perception:

A variety of perceptual-cognitive test procedures have been studied in patients receiving somatic therapies.

a. The Tachistoscopic Perception of Embedded Colored Figures:

This task was studied in an experimental group consisting of 35 consecutive referrals for convulsive therapy, and "control" groups of 20 patients treated with phenothiazine medication (thorazine and promazine) and ten patients receiving no somatic treatment, matched for age. All subjects were tested prior to treatment, and after four weeks; the convulsive patients were tested a third time two weeks following the cessation of treatment.

There was a statistically significant increase in mean number of errors with convulsive therapy, and a significant decrease from the pretreatment scores following treatment. "Control" subjects made significantly fewer errors at each succeeding period. There was a significant difference in errors between patients classified as showing low EEG changes (per cent time delta) when compared with high EEG changes. There were high retest correlations for all groups.

There were marked individual differences in response patterns prior to treatment. With brain changes there was a reduction in perseveration, completion and confabulation in some patients, and an increase in others, with no unique patterns attributed to cerebral dysfunction. Even in those patients with high EEG changes, the "style" of his response pattern was maintained. Thus a patient showing completion type errors prior to treatment would continue to make such errors with convulsive therapy, although the threshold at which completion was shown might change.

(Presented, in part, at the Eastern Psychological Association, Atlantic City, April 1959).

b. Rod and Frame Test (Witkin): This task was administered to 47 patients consecutively referred for somatic therapy. Marked individual differences in performance were correlated with age, education and score on the California F Scale. Patients whose judgment of the vertical was strongly influenced by the surrounding frame (field dependent) were more frequently

referred for convulsive therapy than drug therapy. No significant change was found with drug or convulsive treatment. For both drug and convulsive groups retest correlations were high (+.86 and +.88). It is considered that individual differences on the Rod and Frame test reflect personality factors that are of importance in psychiatric treatment.

B. PSYCHOPHARMACOLOGIC STUDIES.

1. Neurophysiologic Aspects:

According to the neurophysiologic-adaptive view of the convulsive therapy process, the clinical efficacy of repeated induced convulsions is dependent upon the induction of a persistent alteration in central nervous function, providing a milieu for changes in the subject's interaction with the examiner and the environment. In these studies the best index of neurophysiologic change has been those aspects of cerebral function reflected by delta activity in the electroencephalogram (Fink and Kahn, 1957). The efficacy of newer psychopharmaceuticals in altering psychotic behavior patterns has led to the suggestion of a similar hypothesis for the mode of action of these agents, and to studies of the relationship and specificity of altered behavioral patterns to neurophysiologic change as reflected in electroencephalography.

Of the psychopharmaceuticals tested in acute experiments an increase in synchrony with or without an increase in slow wave activity has been observed for chlorpromazine, promazine and trifluprom azine. Behaviorally, these drugs were associated with a) increasing sedation, drowsiness, denial and euphoria; b) decreasing agitation, panic, excitement and delusional and hallucinatory activity; and c) minimization and displacement of symptoms. Barbiturates regularly induced an increase in fast activity with an increase in synchrony, with the associated behavioral changes of sedation, euphoria, denial and minimization.

Amphetamine and methamphetamine increased fast activity without increased synchrony and behaviorally were associated with alerting, hypomania, excitement and increased motor activity. Decrease in voltage and per cent time of slow wave activity in subjects with post-convulsive delta activity was seen with LSD-25, benactyzine, Win-2299, JB-318, JB-336 and diethazine. Of these drugs, benactyzine produced increased alerting, excitement, tension and panic; the other drugs also produced illusory sensations and hallucinatory, delusional and paranoid ideation.

The electrographic patterns were consistently altered concurrently with behavioral changes both in the acute and chronic administration studies. Tranquilization, euphoria, sedation and minimization of symptoms were associated with increased EEG synchronization and shift of frequencies to the delta range. Agitation, tension, panic, excitement, illusions and hallucinations were associated with desynchronization of frequencies.

Similar patterns were demonstrated in subjects with prior delta activity. Agents that tended to synchronize frequencies, as chlorpromazine and barbiturates, augmented the per cent time delta activity and enhanced the clinical patterns; agents that desynchronized frequencies, as diethazine, LSD-25 and benactyzine, minimized the clinical effects typically ascribed to repeated convulsions.

Various experimental psychopharmaceuticals were tested. In addition to extensive studies of b-b methyl ethylglutarimide (Megimide) and hexafluorodiethylether (Indoklon) the following agents were studied; phenyltoloxamine (PRN-Bristol), methonalide (BLM-188, Bristol), tropin-4-chlorbenzhydryl ether (WY-2149, Wyeth), dimethylaminoethanel and its congeners (Deaner and varieties, Riker), JB-318, 329 and 336 (various piperidyl-benzilates, Lakeside) and imipramine (Tofrānil, Geigy).

Because significant behavioral and electrographic changes were observed, a more intensive investigation of imipramine (Tofrānil) was undertaken. In 28 acute experiments, consecutive patients referred for physiodynamic therapies were tested in the EEG laboratory at various stages of treatment. Tofrānil solution (10 mg/cc) was administered intravenously at a set rate (1 cc/40 sec) until electrographic or behavioral changes became prominent, for a total of 40-125 mg (0.5-2.5 mg/kg). Behavioral observation and electrographic recording continued for one to three hours. In patients referred for pharmacotherapy because of manifest depressive, withdrawn or retarded behavior oral Tofrānil of 75-350 mg was administered.

In the acute studies there was initial restlessness, associated with dizziness, dry mouth, "faintness," nausea, and on four occasions, vomiting. These symptoms persisted for 10-20 minutes, and were accompanied by lassitude, heaviness of the extremities and eventual drowsiness. Heart rate was unchanged or slowed. Blood pressure dropped by 20-40% in

older (age ≥ 60) patients. Subsequently, subjects were relaxed, quiet and disinclined to activity, even when returned to their ward.

The electrographoc patterns accompanying these behavioral changes were initiated by a gradual decrease in voltages during the injection. By ten minutes, the per cent time alpha had been halved. In patients with moderate amounts of beta activity, such activity occasionally increased in voltage and per cent time. By twenty minutes, in association with behavioral lassitude, low voltage (to 50 microvolts) random theta frequencies (5-7 cps) appeared. In records with post-convulsive delta activity, there was a marked decrease in voltage and per cent time of slow wave activity. These electrographic patterns persisted for ½ to two hours.

There was considerable individual variability in this acute EEG response. In patients who received 100 mg or more of Tofrānil, EEG and behavioral changes were observed in all but three. In six patients, dosage of Tofrānil less than 50 mg were associated neither with EEG nor with behavioral changes.

In chronic Tofrānil studies, behavioral changes generally appeared during the second, and were maximal during the third, week of treatment. The most prominent behavioral adaptation was euphoric denial. Patients complained less of somatic symptoms, and denied, minimized or displaced their illness on inquiry. It became increasingly difficult to discuss

significant life relationships with them. In six patients somatization and restlessness increased and depressive affect persisted. In three, restlessness, agitation, excitement, insomnia and vomiting, les to the cessation of therapy. No change in symptoms were noted in five patients after four weeks of therapy.

Electrographic studies on chronic administration showed a decrease in voltages with poorer record modulation. Low voltage theta (5-7 cps) activity up to 10% appeared. Well defined fast activity became more prominent in a few.

(Presented at the Collegium Internationale Neuro-Psychopharmacologicum, Rome, September, 1958; at the Conference on Depression and Allied States, Montreal, March, 1959; and American EEG Society, June, 1959. Published, in part, in the Proceedings of C.I.N.P.; Psychopharmacology Frontiers, ed. N. Kline, 325-332, 1959; Canad. Psychiat. Ass. J. 4: 166S-171S,1959; and Neurology 8: 682-685, 1958.

2. Aspects of the Therapist-Patient Relationship Affecting Choice of Therapy.

The selection of therapy involves aspects other than the manifest behavioral patterns of the patient. In the past year further efforts to clarify this problem have been undertaken, emphasizing factors in the therapist-patient relationship. We have hypothesized that frustration and hostility in the therapist-patient relationship and implicit or explicit environmental pressures have a significant influence in referral for somatic therapy.

In a pilot study 76 structured interviews with residents and supervisors were initiated following requests for somato-

therapy. These interviews were designed to elicit the basis of the referral. It was found that in only relatively few cases was there a change in the patient's clinical status which directly led to the referral. In most instances there had been no change or progression in the presenting symptoms. Factors contributing to the timing of the referral included impending discharge, avoiding administrative discharge, and pressure from the patient's family or ward personnel. It was also noted that patients with similar behavior patterns were treated differently, some given somatotherapy and others none. The reasons for this ranged from "whim" to quantitative differences in symptomatology and individual preferences for type of treatment.

It was concluded that factors other than clinical indication played a role in the referral in a significant number of cases. These same extraneous factors also influenced the timing of the referrals.

As a result of these findings a "Somatic Treatment Referral Sheet" was developed (see Appendix) to be completed by the therapist whenever somatic therapy is requested. This study is continuing.

3. Language Patterns as Measures of Behavioral and Neurophysiologic Change with Drugs.

In previous studies of the convulsive therapy process, it was demonstrated that two language measures, a syntactic content analysis (Kahn and Fink, 1958) and dyadic diversification scores of unstructured interviews (Jaffe, Kahn and Fink, 1958) provided objective indices of behavioral change, and were related to the degree of altered brain function. In a further test of these language measures as indices of behavioral and neurophysiologic change, they were applied to interviews on acute administration of various psychopharmacologic agents.

Seventy-two interviews with patients at various stages of drug therapy have been analyzed, using the following agents: amobarbital, benactyzine, chlorpromazine, diethazine, lysergic-acid diethylamide, and Win-2299.

Following a routine electrographic recording, an unstructured psychiatric interview, with short periods of structured inquiry, was tape recorded. With EEG running, an intravenous injection was then given at a slow rate. When specific electrographic or clinical changes were induced, the interview was repeated. Recording periods of EEG and verbal behavior were alternated for the duration of the observation period. The EEG was measured for changes in synchronization, shifts in dominant frequencies, and per cent time of slow waves (delta) and beta frequencies.

The tape recordings were transcribed and measured for the diversification of consecutive 25 word samples of speech of both participants (dyadic) and for syntactic changes. In the dyadic analysis, the pooled verbal behavior of both participants was transcribed, divided into 25 word samples, and for each sample the ratio of the number of different words to the total number of words (a diversification score) was calculated. The syntactic language analyses were based on the response to standardized questions using a method previously described (Kahn and Fink, 1958), scoring such changes as syntactic use of person, alteration in tense, evasion, qualification, displacement or verbal denial of symptoms, use of stereotyped expression or cliches, cryptic response, and withdrawal or silence.

Consistent changes were observed in both the dyadic diversification and syntactic language measures in subjects classified according to the neurophysiologic and behavioral effects of the drugs applied.

Amobarbital and chlorpromazine are neurophysiologic synchronizing agents. Amobarbital regularly induces high voltage well synchronized fast activity at 20-24 cps, while chlorpromazine administration is followed by increased synchronization of the EEG record and a shift to slower frequencies including occasional slow wave burst activity. Behaviorally these drugs are associated with sedation and tranquilization. On the language measures there was an increase in stereotypy

and repetitiveness associated with increasing use of cliches, alterations in tense, displacement and evasion.

Diethazine, benactyzine, LSD-25 and Win-2299 are neurophysiologic desynchronizing compounds. These drugs are characteristically associated with decreased voltage and per cent time of alpha activity and increased irregular low voltage fast activity. Behaviorally hallucinatory, excitatory or illusory activity are observed. On the language measures there was decreasing repetitiveness, wide diversity of words, less variability of diversification scores, and decreased use of cliches and alterations in tense.

Further exploration of language measures are suggested as a rational basis for the understanding of the psychologic effects of the new therapies.

(Presented at the Conference on Psychodynamic, Psychoanalytic and Sociologic Aspects of the Neuroleptic Drugs in Psychiatry, Montreal, April, 1958, and at the American Psychiatric Association, Philadelphia, April, 1959).

SUMMARY

1954 - 1959

The laboratories of the Department of Experimental Psychiatry were established at Hillside Hospital in September, 1954. During this five year period neurophysiologic, psychologic (personality and perceptual), linguistic and sociologic aspects of "somatic" psychiatric therapies have been the principal foci.

1. Convulsive Therapy:

The view of the convulsive therapy process as the induction of a non-specific state of altered brain function, similar to craniocerebral trauma was supported and amplified (10, 11, 21). Within this altered cerebral milieu, subjects were seen to respond in various ways (26), of which the most "successful" was explicit verbal denial (7, 31). This latter adaptation was most prominent in characterologically disposed individuals (36).

An alteration in brain function was pre-requisite to behavioral change (7, 8, 11, 26). Grand mal seizures were essential to this process (26) but electrical induction was not (B-42). The alterations in brain function were measured in various ways including electroencephalography (6, 11, 12, 24, 39), language patterns (4, 7, 14, 31, 43; B-24), perceptual tasks (2, 16, 17, 37, 46; B-26, 41, 42) and tests of

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Reference numbers are to publications or presentations (B-) listed in the appendix.

recall (8).

It was suggested that the neurophysiologic basis of convulsive therapy may lie in an alteration in central synaptic cholinergic - adrenergic relationships, with a predominant shift to increased cholinergic activity as the operationally significant pattern. Such interpretations were based on the relationship of high voltage EEG slow wave activity to behavioral change (6, 11, 26) and the blocking of post-convulsive electrographic and behavioral changes by central anticholinergic agents (21, 34, 35, 41, 42) and central sympathomimetic agents (42).

A variety of behavioral changes were seen during convulsive therapy (26; B-17). Such patterns were viewed as adaptations to altered brain function, and were believed dependent upon characterologic and environmental factors (7, 25, 26, 36, 40). Clinical ratings of improvement were seen as value judgments by the observer of behavioral change in the subject (26). Adaptations characterized by denial mechanisms, both in behavior (B-17) and in language (7, 31) were seen as most favorably rated by the psychiatric staff. Such adaptations were related to habitual modes of conduct (character, personality) (36; B-11, 32).

The persistence of the altered behavioral modes was noted as dependent upon the degree and duration of altered brain function, the environmental expectations, and the type and

degree of family and medical support (26). Different behavioral patterns were best supported by varying types of psychotherapy (19).

Measures of linguistic behavior in structured (7, 31) and unstructured (14, 29; B-24) interviews showed characteristic alterations towards increased denial, minimization, displacement, stereotypy and repetitiveness related to the degree of altered brain function (B-24). These changes were blocked or reversed by anticholinergic hallucinogens (21,43).

Various perceptual tasks provided indices of behavioral change and were related to the degree of altered brain function. These included the perception of simultaneous tactile stimuli (17), embedded (Gottschaldt) figures (37; B-16), and tachistoscopically exposed words (37) and embedded color figures (41).

Sociopsychologic aspects of age, years of education, nativity and degree of stereotypy and conventionality (measured by California F Scale) were related to selection of therapy, duration of hospitalization, diagnosis and treatment response in hospitalized patients (15, 36, 40, 45).

2. <u>Neurophysiologic-Adaptive Hypothesis of Somatic Therapy.</u>

Based on these studies, a hypothesis concerning the mode of action of other therapies such as insulin coma, leucotomy and psychotropic drugs, was expressed (10, 33, 38). This view holds that the efficacy of these therapies depends upon the induction of states of altered brain function, in which

varying adaptive patterns may become prominent. The adaptive pattern is related to the type, degree and duration of altered brain function, the personality of the subject, and tolerances and expectations of the environment.

Examination of this hypothesis as applied to psychotropic drug therapies is now in progress, supported by USPHS grants MY-2092 and MY-2715.

3. Insulin Coma Therapy.

An initial case study showed the significance of denial patterns and of persistent altered brain function for the behavioral changes in insulin coma therapy (3).

In an insulin coma - chlorpromazine control study, no differences in hospital improvement ratings were observed in the two treatment groups (27). Chlorpromazine was safer, easier to administer, permitted continued administration and allowed for greater degrees of concurrent relationship therapy than insulin coma. These observations led to a replacement of insulin coma by psychotropic drugs in this institution.

4. Pharmacotherapy.

The ongoing program in evaluating various psychopharmaceuticals is derived from these hypotheses. Electrographic and linguistic analyses of effects of acute intravenous administration and chronic clinical administration of various new compounds are in progress. EEG patterns, along such continua as synchronization-desynchronization and frequency shift, and various perceptual, perceptual-motor and personality

tasks, are being related to behavioral (21, 34, 41, 42) and linguistic changes (21, 43).

The neurophysiologic basis of experimentally induced hallucinogenic states has been interpreted as an alteration in synaptic chemical relations, such that the effective levels of cholinergic activity is decreased (42). Initial work on this hypothesis (21, 42) is now being expanded.

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9. Modification of Psychotherapeutic and Supervisory Relationships by Altered Brain Function.

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Relation Between Altered Brain Function and Denial in Electroshock Therapy

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Read at the Annual Meeting American Psychiatric Association, May 1955.

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Although many theories concerning the mode of action of electroshock therapy have been offered, the relationships among physiological and psychological factors remain poorly understood (1,2). In previous studies (3,4,5,6) of patients with alterations of brain function, it was suggested that certain of the observed patterns of behavior were related to the therapeutic effects of electroshock.

These patterns included denial of illness or anosognosia (3,6), disorientation for place and time (7), reduplication (8) and changes in language, particularly nonaphasic misnaming or paraphasia (9). It was indicated that these phenomena were forms of adaptation to the stress of illness rather than specific defects in memory, perception or judgment. In the milieu of neural reorganization provided by brain damage, the patient expresses his motivations in new symbolic patterns indicative of changed modes of interaction with the environment. In the anosognosic delusion the patient denies such forms of incapacity as hemiplegia, loss of a limb, blindness, and the fact of an operation, as well as other problems in living. In disorientation for place, the way in which the patient misnames and mislocates the hospital serves as the symbolic representation of some aspect of the traumatic situation, often the need to be well and go home. Thus, he uses the name of a familiar place or locates the hospital close to his home or confabulates a journey outside the hospital. When a paraplegic patient refers to the hospital as a "roller skating academy" or a paranoid patient calls the hospital (Mount Sinai) Mount Cyanide, the names symbolize the patient's feelings in dramatic fashion. In paraphasia, the objects which are misnamed by the patient are usually related to a personal problem, particularly that of illness and hospitalization. Thus, the patient selects aspects of the environment, parts of the body, places and objects and uses them in his language for the expression of his feelings in a new mode of interaction.

could be brought out by the administration of amytal sodium ("positive amytal test"). With a return of the complaints of pain these changes in behavior were no longer apparent either clinically or under amytal. This sequence of events were repeated during two subsequent courses of electroshock. While this report supported the hypothesis regarding the therapeutic action of electroshock and showed the usefulness of the "amytal test" in investigating the problem, it concerned only one case and did not represent the usual condition for which electroshock is given.

The theory is further tested in the present study in which a group of patients receiving electroshock for mental illness were given repeated amytal tests before, during and after the course of treatment. The purpose of the study was to determine the relationship between the clinical response to the treatment and changes in behavior produced by the drug. The particular hypotheses tested were that those patients who improved with electroshock would be more likely to show: (1) evidence of brain dysfunction on the amytal test and (2) behavior patterns indicative of denial.

METHOD

Each patient was given a series of amytal tests. In this test, the patient is asked a standard group of questions pertaining to orientation and the awareness of illness. The drug is then administered intravenously in a 5% solution at a rate of .05 grams (1 cc) per minute until nystagmus, slurred speech, drowsiness and errors in counting backward are noted. The same questions are now repeated. The following changes, when persistent, are called "positive" and are deemed indicative of cerebral dysfunction.

1. Complete denial of illness.
2. Denial of major aspects of illness, such as attributing entry into hospital to a trivial or past illness.
3. Misnaming the hospital, either its proper name, or in terms of a euphemism as "rest home."

4. Displacement of the location of the hospital, such as to another city.

5. Confabulated journey.

6. Reduplication of the hospital, as stating that he is in another hospital of the same or similar name.

7. Disorientation for time of day with confusion of day and night.

8. Gross misidentification of the examiner such as calling him a "lawyer" or an "entertainer".

9. Disorientation for year.

The patient was given his first test prior to treatment, and re-tested at weekly intervals. All patients in the series had negative amytal tests prior to the initiation of therapy. Treatments were administered three times a week, so that the patients were generally tested after every third treatment. A test was always given two days after a treatment. Testing was continued after the termination of therapy until the result had become negative.

Electroencephalographic records and standard tests of memory and learning ability were also given, but will not be considered in detail in this paper.

POPULATION

Twenty-four patients at Hillside Hospital receiving electroshock with the Reiter Electrostimulator were studied. There was no selection of cases by the authors. The patients were taken on the basis of consecutive referrals, and the determination of the necessity for treatment was made by the clinical staff. Some patients were necessarily excluded because their treatment was terminated or interrupted before they were adequately studied. Another was omitted because he had manifestations of brain disease and a positive amytal test prior to electroconvulsive therapy. The number of treatments varied from nine to thirty-three. Patients who showed clinical improvement tended to receive fewer treatments. Some of this variability could also be ascribed to differences in the inclination of the resident psychiatrists to use this form of treatment.

One patient decided for himself that he had enough treatment and eloped. Diagnostically, the patients consisted of 14 with depressive reactions, 9 with schizophrenia and one manic reaction. There were 15 women and 9 men in the series, and the ages ranged from 24 to 68 with a median of 47.

Evaluation of response to E.S.T.

All the patients were observed for at least eight weeks after completion of treatment. Determination of the patient's response to electroshock was made on the basis of the resident psychiatrist's impression, staff opinion, the nurses' notes and the clinical evaluation of one of us (M.F.) who supervised the treatments but was not aware of the amytal test results. In this way the patients were classified into three groups.

A. Markedly Improved. The 11 cases in this group were regarded as showing recovery or marked improvement. These patients no longer showed the symptoms which brought them into the hospital; their doctors felt they were better; and the nurses' notes confirmed such aspects as being able to sleep without medication, better appetite, and improved capacity to get along with the other patients and participate in hospital activities.

B. Moderately Improved. The six patients in this group showed some improvement but continued to manifest indications of mental illness. These patients typically showed symptomatic relief, i.e., acute depressive features might be gone, but the dramatic change so evident in the first group was not apparent. Each patient continued to show some noticeable disturbance such as obsessional thinking, paranoid ideas, or somatic preoccupation.

C. Minimally or Unimproved. In this group were placed seven patients in whom change was not clearly noticable or who showed only equivocal or transient improvement. Some showed fluctuations in behavior, at times appearing somewhat improved. But the change was not sustained, so that by the end of

treatment, they appeared much as they did before.

We are aware of the difficulties in evaluating improvement. Others might have differed in the estimates of change in these patients. In any case, by using this threefold classification, the differences between the first and third groups will be distinct.

OBSERVATIONS

1. Amytal Test Results

A. Distribution of Positive Reactions. The number of amytal tests given to each patient during the course of electroshock ranged from three to thirteen, depending on how long treatment was maintained. In Table I, the data is shown for the number of tests given during treatment and the number and percent positive for all the patients in each group. The markedly improved patients showed many more positive reactions than the unimproved group, with the moderately improved patients in between these groups. Every markedly improved patient had at least one positive amytal reaction during treatment. On the other hand, one of the moderately improved patients and five of the unimproved cases never showed a positive result. A comparison of the results in each of the groups, using chi-square, is statistically significant at better than the 1% level of confidence.

TABLE I

DISTRIBUTION OF POSITIVE AMYTAL TESTS DURING TREATMENT

	No. of tests given during treatment	Number positive	% Positive
Markedly improved (11)	50	38	76%
Moderately improved (6)	39	15	38%
Unimproved (7)	45	6	13%

B. Positive reactions at each stage of treatment. In Fig. 1 the groups are compared for the percentage of patients in each group who had positive

results at each stage of treatment.

Almost half the markedly improved patients had positive reactions after only three treatments, and all had positive reactions after seven to nine treatments. In the unimproved cases, on the other hand, the number of positive reactions was small and there was no consistent increase during the course of treatment. Again, the moderately improved group tends to fall between the other two.

Although some patients received more than 15 treatments the data is not presented beyond this point because the number in each group became too small for purposes of comparison. Four of the unimproved patients received more than 20 treatments with consistently negative amytal test results. One of the moderately improved patients received over 30 treatments with only an occasionally positive reaction.

C. Duration of positive reactions. There were variations in the persistence of positive reactions from week to week. Using at least two consecutive positives as the criterion of persistence, nine of the markedly improved, two of the moderately improved and only one of the unimproved group showed persistent positives. After the termination of treatment all patients but one had negative amytal reactions nine days after the last convulsion. The remaining patient developed a negative test by the second week after treatment.

D. Factor of age. Since the patients in the markedly improved group tended to be older persons suffering from depressive reactions, it is conceivable that the difference in amytal test results might be related soley to age and only coincidentally to clinical improvement. Underlying this is the assumption that the older person is more likely to show signs of altered brain function when given electroshock. In Table 2 the mean age for each group is shown.

TABLE 2

RELATIONSHIP OF CLINICAL IMPROVEMENT TO AGE

	Mean Age
Markedly Improved (11)	47.64
Moderately Improved (6)	50.00
Unimproved (7)	35.29

It is apparent that the first two groups were older than the unimproved patients. Yet, while the mean age of the moderately improved cases is slightly higher than the markedly improved group, these patients still show significantly fewer positive reactions.

In Table 3 the number of positive reactions during treatment is shown for each group when the analysis is limited to patients over 40 years of age. In this table the relationship of positive reactions in the different groups remains unchanged from that when the groups are considered as a whole.

TABLE 3

DISTRIBUTION OF POSITIVE AMYTAL TESTS IN PATIENTS OVER 40

	No. of tests given during treatment	Number positive	% Positive
Markedly Improved (10)	46	35	76
Moderately Improved (5)	34	15	45
Unimproved (3)	17	0	0

2. Other Aspects of Behavior.

Apart from explicit denial of illness and disorientation there were changes in behavior that occurred both under the influence of the drug and clinically during the course of treatment is significantly progressive fashion in those patients who improved. These aspects may be divided into verbal and non-verbal communication.

A. Changes in Verbal Language. These consisted of denial expressed in

evasion and in the use of a syntactical pattern involving the third and second person. When asked about their symptoms patients gave such answers as "it's hard to say" or "I forgot" or "I don't know; I've been waiting for the doctors to tell me." The change in syntactical person is illustrated by such remarks as "it's what they call a depression," "I'm afraid somebody will get hurt" or answering the question "what is your main trouble" with "what is your main trouble." Sometimes patients would talk of a relative who was sick.

In patients who improved there was a notable development of such patterns in the non-drug interviews. One such patient, for example, when asked prior to the start of treatment what was his main trouble, said "I'm depressed." After two treatments he answered the question with "I don't get along well with my mother-in-law." After five treatments he said "I don't get what you mean," and after eight, "I get sick; that's all I know." After ten he said "right now, it's that I don't see my wife," and after 11 said "in what way do you mean" and "I don't know how to explain it." At the termination of treatment, his main trouble was given as "I want to get home" followed by an account of how "good" his wife was.

In the unimproved group, on the other hand, the increased use of these language patterns did not occur. They were not present in some, minimally or inconsistently noted in others. In some of the unimproved patients there was actually less use of these language patterns under the effects of the drug than there had been in the pre-amytal interview.

B. Changes in Non-Verbal Behavior. Euphoric reactions occurred both in clinical and drug interviews most frequently in the markedly improved, less in the moderately improved and least in the group which were considered unimproved. In the unimproved patient classed as manic, euphoric behavior was present in his clinical behavior and was not changed by amytal.

Changes in sexual behavior appeared in the amytal interviews of four of the markedly improved patients but in only one patient in each of the other categories. This took the form of trying to hug or caress the examiner, making remarks with sexual content or engaging in masturbatory activity. A patient in the unimproved group showed this behavior both during pre-drug interviews and under the influence of amytal.

Withdrawal or "selective inattention" was shown by nine of the eleven markedly improved patients particularly during the drug phase of the amytal interview. This behavior consisted of failure to answer the questions about illness and hospitalization or responding in dysarthric and cryptic fashion. This reaction under the drug occurred only once in each of the other groups. It was of interest that two patients in the unimproved category who appeared withdrawn before the test became more responsive under the influence of the drug.

DISCUSSION

The results of the amytal tests in these patients indicate that there is a relation between clinical improvement and the production of brain damage or an altered state of brain function as determined by this particular method of examination. In patients who improve, the amytal test becomes consistently positive early in the course of treatment. In moderately improved or unimproved patients there are fewer positive reactions and their frequency does not increase with more treatments. With other methods of evaluating brain function such close correlation was not present. All patients showed abnormalities in the electroencephalographic record * and impaired learning was found as frequently in patients who improved as in those who did not. The effects of brain damage are not unitary and different methods of study show varying results.

* The electroencephalographic data in these patients are being analyzed in more detail, and will be reported elsewhere. The preliminary findings show that the degree of EEG abnormality is related to improvement, comparable to the amytal test findings.

In relating the various aspects of altered brain function to changes in behavior after electroshock therapy it has been helpful to distinguish between defects in the formation of symbol patterns and defects in the adaptive uses of language. In the first category one may include such clinical phenomena as aphasia, apraxia, finger agnosia, acalculia and certain types of memory loss. In aphasia, the patient may "know" what he wants to say but he cannot select the appropriate elements from the entire category of sounds and movements and integrate them. With memory defects the patient cannot select elements of experience, class them into significant units and arrange them in a temporal pattern. Such defects are also commonly manifested in tests of problem solving and in certain subtests of the Wechsler-Bellevue scale. Such patients are frequently concerned with their defects and exhibit marked degrees of anxiety and frustration.

Adaptive changes in language, on the other hand, relate to interaction with the environment and concern the motivational aspects of behavior. They are exemplified in the phenomena of denial and disorientation. The same behavioral element may appear under certain conditions as a defect and in other cases as a form of adaptation. Left-right disorientation, for example, may be part of an aphasic defect in which the concept of left and right is impaired or lost. Other patients, however, may not seem able to identify a paralyzed left arm, but can show their (non-paralyzed) right arm and their left ear or similarly indicate a knowledge of left and right as long as it does not relate to their illness. The therapeutic action of electroshock is not in the production of defects in symbol formation but rather in providing the neural milieu in which altered forms of adaptation may be maintained.

Many psychiatrists predict the outcome of electroshock treatment by the amount of "confusion" that occurs after the initial treatments. Other point to cases where "confusion" was not related to improvement. The amytal test

should be useful as a prognostic guide by defining the nature of these changes. In some cases "confusion" may be mainly a matter of memory defect and in these patients the amytal test may be negative. On the other hand, some patients improve after a few treatments without clinical evidence of "confusion." In such instances the amytal procedure may show an alteration in brain function. In this study almost half of the markedly improved patients had positive reactions within three treatments. In another case, treated privately by one of us (E.A.W.), marked improvement of a severe depressed condition was noted after only two convulsions. Yet this patient, who had a negative amytal result prior to treatment, showed a markedly positive reaction one day after the second treatment.

These results do not mean that improved patients have a greater degree of brain damage than patients who do not improve. The amytal test does not directly measure brain damage, but rather one deduces the presence of brain damage from the nature of the adaptive changes in communication. Thus patients with brain damage who do not show such changes are considered to show a negative result. It is for this reason that other behavioral methods of demonstrating impaired brain function may not distinguish between improved and unimproved patients. Why some patients develop a positive amytal test, and others do not despite many more convulsions is unclear, but may be related to personality factors and to the patient's habitual mode of adaptation to stress. It is necessary, nevertheless, that a state of altered brain function be created so that these forms of adaptation or denial can be maintained. It is for these reasons that it is believed that methods of administering electroshock which alter brain function minimally as unilateral seizures will not be generally efficacious. Also it affords some explanation as to why electroshock often has a beneficial short term effect while evaluation of long term effects show little difference between treated and untreated cases.

In considering what constitutes "improvement," it is likely that such evaluations are dependent in considerable degree on the types of verbal and non-verbal adaptation that the patient uses. Thus, when a patient denies that he has any problems, and appears affable and uncomplaining, he is rated improved. It does not mean that he has acquired insight or that he has developed a more realistic understanding of his interpersonal relations. This is well exemplified by the patient previously cited who said he was "depressed" in the pre-treatment interview, but later used evasion and use of the third person when asked about his illness. While his behavior is rated as improved, actual analysis of his language shows that he is using different forms of symbolic adaptation.

Recent studies have supported the findings concerning the development of mechanisms of denial in the improved patients. Carter (12) confirmed Janis' (13) findings of consistent evidence of circumscribed amnesias in patients following electroshock. He concluded that general memory impairment did not occur, but rather, that there was a "selectivity" in forgetting of unpleasant material from the patient's past life. Korngold (14) likewise reports selective and highly sensitized forgetting. Teicher (15) similarly, observes "mechanisms of repression" for "emotional" stimuli after electroshock.

Another aspect of the difference between the improved and unimproved groups which may bear a relation to the therapeutic mechanism was that in improved patients there were more changes in <u>all</u> types of symbolic adaptation, not only in verbal patterns. Thus, a patient who appeared withdrawn both in the pre-drug and drug interviews had a poorer prognosis than the patient who became withdrawn only under the effects of the drug. Similarly, the patient who showed altered sexual behavior under the effects of the drug had exhibited this behavior during the pre-amytal questioning as well, and did not improve with treatment, while the four patients manifesting sexual behavior only under

the effects of the drug, did improve. The importance of the change in symbolic pattern is also illustrated by the fact that the unimproved manic patient showed no changes in this aspect of his behavior during the amytal test. It is thus likely that the facility of changing symbolic patterns in a situation of added stress is an important one in determining response in all somatic therapies.

SUMMARY AND CONCLUSIONS

(1) Twenty-four patients referred consecutively for electroshock treatment were given amytal tests before, during and at regular intervals during the course of treatment.

(2) There proved to be a close relationship between the short-term response to treatment and the results of the amytal tests. The much improved patients showed early, persistent and increasingly positive reactions during the course of treatment. Unimproved patients showed no positive reactions or showed them infrequently and inconsistently. An intermediate group who showed moderate clinical improvement showed more positive reactions than the unimproved group but fell far short of the much improved in the incidence of positive reactions.

(3) Changes in language and non-verbal forms of behavior related to denial were most consistent and pronounced in the improved group, even in interviews not employing drugs.

(4) The observations support the hypothesis that clinical improvement in electroshock requires the creation of a milieu of altered brain function in which new patterns of adaptation, particularly those of denial, may be maintained.

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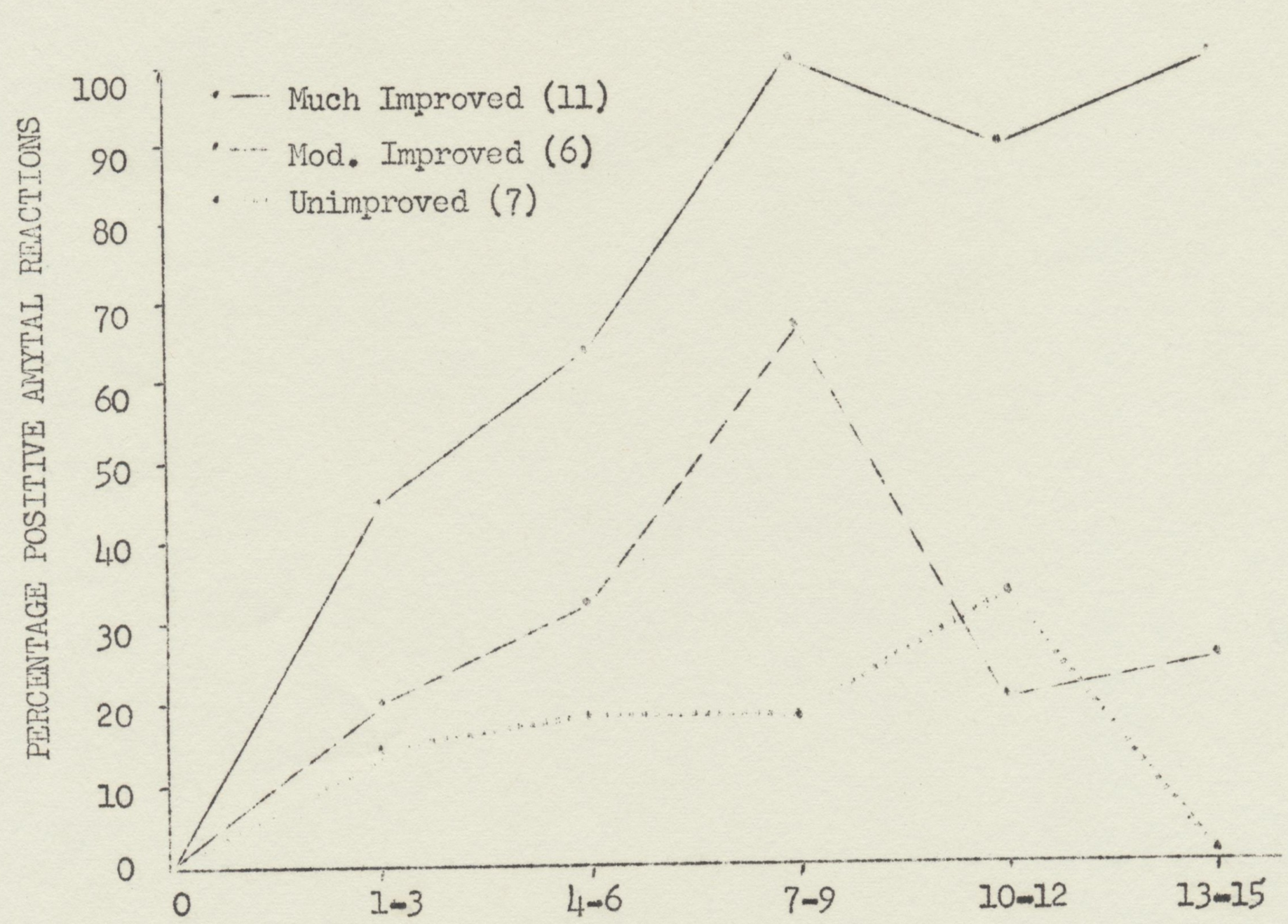

Fig. I.— Percentage of positive amytal test reactions occurring in each group at different stages of treatment.

Provisional Report
RLK

JUN 26 1959

Altered Brain Function Following Electroshock

M-927

Progress Report - February 1 1958 - September 1 1959

Summary:

In the past eighteen months various studies of the convulsive therapy process were completed, a program for the investigation of psychopharmacologic agents consistent with the general hypothesis concerning the mode of action of physiodynamic therapies was developed. The interrelationship of the neuro-physiologic effects of many new compounds with the psychodynamic, perceptual, personality and sociologic aspects of patients' behavior provided the framework for these investigations. The following areas of study were explained: 1) the interrelation of psychotherapy with physiodynamic therapy; 2) the elucidation of the synaptic chemical events which are the basis of the convulsive therapy process by the acute administration of experimental anticholinergic compounds at various stages of convulsive therapy; 3) studies of the acute and clinical EEG and behavioral effects of a variety of psychopharmacologic agents; 4) the use of language indices, such as syntactic and dyadic-

diversification analyses, as measures of behavioral and neurophysiologic changes with drugs; 5) a comparative study of indoklon and electrically-induced convulsions in psychiatric therapy; 6) sociopsychologic aspects related to duration of hospitalization, discharge ratings and diagnosis in a voluntary mental hospital; 7) the relation of social attitude to the effects of convulsive therapy; 8) aspects of the therapist-patient relationship affecting ~~xhmxm~~ choice of therapy; 9) studies of individual differences in the selection of, and behavioral change with, convulsive therapy by perceptual methods.

These studies have supported and expanded the neuro-physiologic-adapative view of convulsive therapy, and demonstrated that such a hypothesis has applicability to our understanding of the mode of action of psychopharmacologic agents.

Progress Report:

A. Psychotherapy and Physiodynamic Therapy.

Previous observations have shown that two types of patients are referred for electroshock in this hospital. The largest number are patients in the older age groups who have limited education and are foreign born. They tend to be non-introspective persons, stereotyped in their thinking and language and verbally uncommunicative. Their predominant symptoms are depression, agitation, withdrawal and somatization. The second, and smaller, group of patients are younger, native-born, better educated, and verbally communicative with a capacity for introspection. They characteristically exhibit thinking disorders and overactive behavior states, with somatization and depression occurring to a lesser extent.

An explanatory study was undertaken of four patients, two for each group described above, for the purpose of determining 1) reasons for referral for convulsive therapy, 2) whether the differences in patients required different attitudes in psychotherapeutic management with electroshock, and 3) the

relation of the psychotherapeutic approach to the patient's clinical response to electroshock.

It was found that all of the patients studied were referred for electroshock because of a failure of communication in the psychotherapeutic relationship. In two cases this was a reflection of the limited verbal and introspective capacity of the patientdue to educational and social factors. In the other two cases, however, the impaired communication was primarily due to unmanageable acting out.

Following treatment, the older, less educated patients were able to maintain this improvement with a reassuring technique, supporting the tendencies to minimization and denial developed during electroshock. In the better educated patients, electroshock seemed to make the patients more amenable to an interpretive form of psychotherapy.

It was concluded that the relationship of psychotherapy to electroshock varies with the particular type of communication pattern and adaptation shown by the individual patient. This

material has been written up and published in the Journal of Hillside Hospital, 7: 17-25, 1958.

B. Biochemical Aspects of the Convulsive Therapy Process.

The significance of high voltage EEG delta activity in the convulsive therapy process (Roth et al, 1951, 1957; Fink and Kahn, 1957) and the report that this delta activity was blocked by the administration of anticholinergic compounds, atropine and scopolamine (Ulett and Johnson, 1957) provided the basis for these studies. As there were attendant unpleasant systemic effects with the administration of these agents, reports describing diethazine as an anticholinergic compound with potent neurologic but minimal systemic effects (Jenkner and Lechner, 1955; Lechner, 1956) led us to undertake studies similar to those of Ulett and Johnson using this compound (Fink, 1958). These observations with diethazine led to the investigation of other experimental anticholinergic agents.

Clinical and electroencephalographic responses to the intravenous administration of various anticholinergic agents

in psychiatric patients at various stages of convulsive therapy were studied. These observations were related to hypothesis covering the mode of action of convulsive therapy and of hallucinogens.

The subjects were ninety psychiatric patients referred for convulsive therapy, ranging in age from 18 to 67, with a variety of diagnoses. A total of 107 observations were made, since some subjects were studied with more than one compound.

The drugs were administered at various stages of the treatment process. The observations were made in the EEG laboratory using a standard 8 channel instrument and needle electrodes. In each trial, the compound under study was administered intravenously at a set rate per minute with clinical behavior until or electrographic changes were observed.

The compounds studied have been diethazine, Win-2299, benactyzine, JB-318, JB-336, and atropine. Each is a potent anticholinergic agent <u>in vitro.</u>

It was observed that diethazine, Win-2299, benactyzine,

JB-318 or JB-336 administration at various stages of convulsive therapy were associated with a) desynchronization of EEG rhythms with a blocking of post-convulsive delta activity; b) alerting, excitatory behavioral response with illusory, delusional and hallucinatory ideation, and c) systemic effects of muscular weakness, degrees of the mouth, dry skin and tachycardia. The electrographic, behavioral and systemic effects were concurrent.

These observations are regarded as consistent with the suggestion that the physiologic basis of convulsive therapy lies in an increase in central nervous system cholinergic activity.

Observations that LSD, amphetamine, mescaline and diphenhydramine- sympathomimetic and antihistaminic agents - also induce EEG desynchronization, blocking of post convulsive delta activity and clinical excitatory activity support the suggestion that both the behavioral and electrographic patterns are based on alteration in synaptic activity. Increased synaptic activity (cholinergic, sympatholytic effects) is

associated with EEG hypersynchronization, and clinical sedation and euphoria; while decreased synaptic activity (anticholinergic, sympathomimetxic) is associated with EEG desynchronization and clinical excitatory and hallucinogenic states.

Discrepant observations with the anticholinergic agents, atropine, are considered to be related to significant differences in dosage and structural chemistry.

This material was presented at a meeting of the American EEG Society in Atlantic City, June 14, 1958.

C. Acute and Chronic EEG and Behavioral Effects of Psychopharmacologic Agents.

According to our neurophysiologic-adaptive view of the convulsive therapy process, the clinical efficacy of repeated induced convulsions is dependent upon the induction of a persistent alteration in central function, providing a milieu for changes in the subject's interaction with the examiner. In our studies the best index of neurophysiologic change has been those aspects of cerebral function reflected by delta activity in the electroencephalogram (Fink and Kahn, 1957).

The efficacy of newer psychopharmaceuticals in altering psychotic behavior patterns has led to the suggestion of a similar hypothesis for the mode of action of these agents, and to studies of the relationship and specificity of altered behavioral patterns to neurophysiologic change as reflected in electroencephalography.

Of the psychopharmaceuticals tested in acute experiments an increase in synchrony with or without an increase in slow wave activity has been observed for chlorpromazine, promazine and trifluprom azine. Behaviorally, these drugs were associated

with a) increasing sedation, drowsiness, denial and euphoria; b) decreasing agitation, panic, excitement and delusional and hallucinatory activity; and c) minimization and displacement of symptoms. Barbiturates regularly induced an increase in fast activity with an increase in synchrony, with the associated behavioral changes of sedation, euphoria, denial and minimization. Amphetamine and methamphetamine increased fast activity without increased synchrony; behaviorally they resulted in behavioral alerting, hypomania, excitement and increased motor activity. Decrease in voltage and per cent time of slow wave activity in subjects with post-convulsive delta activity was seen with LSD-25, benactyzine, Win-2299, JB-318, JB-336 and diethazine. Of these drugs, benactyzine produced increased alerting, excitement, tension and panic; the other drugs also produced illusory sensations and hallucinatory, delusional and paranoid ideation.

The electrographic patterns were consistently altered concurrently with behavioral changes both in the acute and chronic administration studies. Tranquilization, euphoria,

sedation and minimization of symptoms were conversely associated with increased EEG synchronization and shift of frequencies to the delta range. Agitation, tension, panic, excitement, illusions and hallucinations were associated with desynchronization of freqnencies.

Similar patterns were demonstrated in subjects with prior delta activity. Agents that tended to synchronize frequencies, as chlorpromazine and barbiturates, augmented the per cent time delta activity and enhanced clinical pattern; agents that desynchronized frequencies, as diethazine, LSD-25 and benactyzine, minimized the clinical effects typically ascribed to repeated convulsions.

Following these preliminary observations more intensive investigation of an agent, imipramine (Tofranil), was undertaken. In 28 acute experiments, convulsive patients referred for physiodynamic therapies were tested in the EEG laboratory at various stages of treatment. Tofranil solution (10 mg/cc) was administered intravenously at a set rate(1 cc/40 sec) until electroencephalographic

or behavioral changes became prominent, for a total of 40-125 mg (.05-2.5 mg/kg). Behavioral observation and electrographic recording continued for one to three hours. A second group of 16 patients manifesting depressive, withdrawn or retarded behavior and who were referred for pharmacotherapy, received daily oral Tofranil of 75-250 mg for four weeks or longer.

In the acute studies there was initial restlessness, associated with dizziness, dry mouth, "faintness," nausea, and on four occasions, vomiting. These symptoms persisted for 10-20 minutes, and were accompanied by lassitude, heaviness of the extremities and eventual drowsiness. Heart rate was unchanged or slowed. Subsequently, subjects were relaxed, quiet and disinclined to activity, even when returned to their ward.

The electrographic pattern accompanying these behavioral changes were initiated by a gradual decrease in voltages during the injection. By ten minutes, the per cent time alpha had been halved. In four patients with moderate amounts of beta activity, such activity increased in voltage and per cent time. By twenty

minutes, in association with behavioral lassitude, low voltage (to 50 microvolts) random theta frequencies (5-7 cps) appeared. In six records with post-convulsive delta activity, there was a marked decrease in voltage and per cent time of slow wave activity. These electrographic patterns persisted for ½ to two hours.

There was considerable individual variability in the acute EEG response. In patients who received 100 mg or more of Tofranil, EEG and behavioral changes were observed in all but three. In six patients, dosage of Tofranil less than 50 mg were associated with either EEG or behavioral changes.

In the chronic Tofranil studies behavioral changes generally appeared during the second, and were maximal during the third, week of treatment. The most prominent behavioral adaptation was euphoric denial which was noted in eight patients. They complained less of somatic symptoms, and denied, minimized or displaced their illness on inquiry. It became increasingly difficult to discuss significant life relationships with them.

in three patients somatization and restlessness increased and depressive affect persisted. In two of these, restlessness, insomnia and vomiting led to cessation of therapy. No change in symptoms were noted in five patients after four weeks of therapy.

Electrographic studies on chronic administration showed minimal changes. Voltages became lower and record modulation poorer. Well defined fast activity became more prominent, and in four subjects, low voltage theta (5-7 cps) activity was noted. ## Details of these studies were presented at the Collegium Internationale Neuro-Psychopharmacologicum, Rome, September 12, 1958, and at the Conference on Depression and Allied States, Montreal, March 19-21, 1959.

D. Language Patterns as Measures of Behavioral and Neurcphsyiologic Change with Drugs.

In previous studies of the convulsive therapy process, it was demonstrated that two language measures, syntactic content analysis ( ) and dyadic diversification in interviews ( ) provided objective indices of behavioral change, and were related to the degree of altered brain function. In a further

test of language measures as indices of behavioral and neurophysiologic change, they were next applied to recordings of interviews on acute administration of various psychopharmacologic agents.

At the present time 72 interviews with patients at various stages of drug therapy have been analyzed, using the following agents: amobarbital, benactyzine, chlorpromazine, diethazine, lysergic-acid diethylamide, and Win-2299.

Following a routine electrographic recording, an unstructured ~~physiologic~~ psychiatric interview, with slow periods of structured inquiry, was tape recorded. With EEG running, an intravenous injection was then given at a slow rate. When specific electrographic or clinical changes were induced, the interview was repeated. Recording periods of EEG and verbal behavior were alternated for the duration of the observation period.

The EEG was measured for changes in synchronization, shifts in dominant frequencies, and per cent time of slow waves (delta and beta frequencies.

The tape recordings were transcribed and measured for the diversification of consecutive 25 word samples of dyadic speech and for syntactical changes. In the dyadid analysis, the pooled verbal behavior of both participants was transcribed, divided into 25 word samples, and for each sample a diversification score was calculated, i.e., the ratio of the number of different words to the total number of words.

The syntactic language analysis were based on response to standardized questions using the method previously described ( ), scoring such changes as syntactical use of person, alteration in tense, evasion, qualification, displacement or verbal denial of symptoms, use of stereotyped expression or cliches, cryptic response, and withdrawal or silence.

Consistent changes were observed in both the dyadic diversification and syntactic language measures in subjects classified according to the neurophysiologic and behavioral effects of the drugs applied.

Amobarbital and chlorpromazine are neurophysiologic synchronizing agents; amobarbital regularly induced high voltage

well synchronized fast activity, at 20-24 cps, while chlorpromazine administration was followed by increased synchroniziation of the EEG record and a shift to slower frequencies including occasional slow wave burst activity. Behaviorally these drugs are associated with sedation and tranquilization. On the language measures there was an increase in stereotypy and repetitiveness associated with increasing use of cliches, alterations in tense, displacement and evasion.

Diethazine, benactyzine, LSD-25 and Win-2299 are examples of the neurophysiologic desynchronizing compounds. These drugs characteristically induce decreased voltage and per cent time of alpha activity and increased irregular low voltage fast activity. Behaviorally they are associated with hallucinatory, excitatory or illusory activity. On the language measures they induced decreasing repetitiveness, wider diversity of words, less variability of diversification scores, and decreased use of cliches and alterations in tense.

Further exploration of language measures are suggested as a rational basis for the understanding of the psychologic

effects of the new therapies.

Details of these studies have been presented at the Conference on Psychodynamic, Psychoanalytic and Sociologic Aspects of the Neuroleptic Drugs in Psychiatry, Montreal, April 11-13, 1958, and at the American Psychiatric Association, Philadelphia, April 27, 1959.

E. A Comparable Study of Indoklon and Electrically-Induced Convulsions in Psychiatric Therapy.

In our investigation of the mode of action of convulsive therapy we have previously conducted a convulsive-subconvulsive control study. This study demonstrated that a significant behavioral change occurred almost exclusively in patients receiving grand mal electroconvulsive therapy. The present report is an assessment of the relative neurophysiological behavioral and clinical effects of two different methods of inducing convulsions - electrical (alternating current) and inhalent (indoklon).

Twenty-five consecutive patients referred for convulsive therapy were studied. They were randomly divided into two groups, 13 patients receiving grand mal therapy induced by the standard Medcraft alternating current instrument, while convulsions were induced in the remaining 12 by the inhalation of hexafluorodiethyl-ether (indoklon). In both groups treatment was administered three time a week for a total of 10 to 24 applications, determined on the basis of clinical criteria by the supervising psychiatrist.

All patients were tested one to two days prior to the first treatment, following 10-12 treatments, and two weeks following the last treatment. The tests given included measures of intellectual functioning (five subtests from the Wechsler-Bellevue Intelligence Scale), perception (figure-ground discrimination using embedded geometric figures, the perception of pseuoisochromatic color plates at high speeds of tachistoscopic exposure, and the Street incomplete figures test), and social attitude (the Levinson revision of the California F Scale).

An EEG was given during each of the testing periods.

The per cent time slow wave activity from a continuum 66 second sample was used as the index of neurophysiologic change.

The results failed to show any significant intergroup test differences between the electroshock and indoklon groups at each of the three test periods. Intragroup analysis, however, showed that during treatment both groups made increased errors on the intellectual and peripheral tests, and had high scores on the F scale. By two weeks after the termination of treatment both groups returned to near pretreatment levels for most tests.

Both groups were comparable for the degree of induced slow wave activity in the EEG after 10-12 treatments. The mean per cent time delta for the indoklon group was 51%, and for the electroshock group 47.5%. Within each group individual differences in behavioral change were related to the degree of physiologic change, those with the highest per cent time delta showing the greatest behavioral change. Rank and correlation between change in test performance and degree of slow wave activity with treatment were positive for all procedures, except the comprehension subtest of the Wechsler-Bellevue, and reached a level of statistical significance for Digit Span (ρ .61, $p < .01$),

object Assembly (+.46, $p < .05$), F scale (+.38, $p < .05$), tachistoscopic perception (+.67, $p < .01$) and perception of embedded figures (+.43, $p < .05$).

This study has demonstrated that two very different convulsant agents may produce similar neurophysiologic and behavioral change. It is concluded that behavioral changes in convulsive therapy are related to the degree of altered brain function, and are non-specific for the type of agent used to induce the convulsion.

Details of this study were presented at the Eastern Psychological Association in Atlantic City, April, 1959.

F. Sociopsychological Aspects of Psychiatric Treatment.

In a previous study of the Hillside Hospital population, it was shown that the factors of age, education, place of birth and social attitudes as measured by the California F scale, were related to the selection of therapy. Those patients who were older, had less education, were foreign-born and with high stereotypy scores on the F scales were more likely to receive

convulsive therapy. In contrast, patients who were younger, better educated, native-born and obtained low scores on the F scale, received psychotherapy as their sole form of treatment.

Further study was undertaken to determine the relation of sociopsychological factors to 1) the duration of hospitalization, 2) the clinical evaluations at time of discharge, and 3) the final diagnosis.

The entire in-patient adult population of Hillside Hospital on March 7, 1957 was studied. This consisted of 171 patients, 57 men and 114 women, ranging in age from 16 to 68 years, with a median of 35 years.

It was found that patients hospitalized for the shortest period (1-5 months) were oldest, had the least education, were most likely to have been foreign-born, and had the highest scores on the F scale. Younger, native-born, more educated, lower F score patients were hospitalized the longest (10 or more months). The same relationship of these factors to length of hospitalization was found when separate analyses were made

according to diagnosis and type of treatment (convulsive therapy or psychotherapy).

Discharge evaluations of improvement in the total population studied were significantly related to age, the older patients having the most favorable ratings. Analysis of the data by type of treatment, however, demonstrated that among the convulsive therapy patients ratings of recovered or much improved were given to those patients with the highest F scores, least education and who were foreign-born.

Diagnoses of schizophrenia or psychoneurosis were associated with lower F scores, younger ages, more education and native birth. The older, less educated, foreign-born, high F score patients were more frequently classified as involutional or manic-depressive psychosis.

It is postulated that these relationships reflect the influence of social background on psychological processes, such as the behavioral patterns of communication, modes of expression and symbolic values. These not only contribute to the pattern of mental illness, but affect all aspects of

the patient-therapist interaction.

Details of this study have been presented at the Eastern Psychological Association in Atlantic City, April, 1959, and at the Academy of Psychoanalysis in Philadelphia, April 26, 1959, and has been accepted for publication in the Archives of General Psychiatry.

G. The Relation of Social Attitude to the Effects of Convulsive Therapy.

As indicated in the previous section, the California F scale has been found useful in understanding factors related to the referral for convulsive therapy and the evaluation of clinical response following such treatment. Further studies have been undertaken with this scale in regard to the following questions: 1) What does the F scale measure in our psychiatric population? 2) What are the behavioral changes induced with convulsive therapy? 3) How are these changes related to the degree of altered brain function?

To answer the first question, in part, the entire in-patient population of the hospital was given the F scale. One month later they were retested with a "reverse" F scale, in which each statement was changed to the opposite of the original. The "reverse" scale was scored in the same manner as the conventional scale, with high scores reflecting greater agreement. The purpose of this procedure was to determine whether the patients' responses were related to the contents of the statements, or were a manifestation of a more general personality aspect, such as acquiescence.

It was found that those patients who made low scores originally, indicating predominant disagreement with the statements, showed a large increase on the "reverse" scale, indicating a high degree of agreement. In contrast, patients who made high scores initially showed little change on retesting, agreeing with the statements to the same extent even though the meaning was reversed. It is evident that, in our population, low F score patients are more critical and discriminating persons, while those with high F scores are more undifferentiating and

and stereotyped in their reactions.

This observation is related to the process of selection of patients for convulsive therapy. A high degree of stereotypy of thinking and communication is incompatable with the establishment of a conventional psychotherapeutic relationship, preventing the psychoanalytically-oriented psychotherapy stressed at Hillside Hospital. It follows that the high F score patients will be unsuccessful in psychotherapy and most likely referred for convulsive therapy.

To answer the second and third questions raised above, 69 patients were given the F scale before, during (at 10-12 treatment period) and after convulsive therapy. Ten of these patients, selected at random, constituted the control group and received subconvulsive electrostimulation. There was a mean increase of *5.7 during treatment in the convulsive group, a difference significant at the 5% level. In contrast, the control group showed an insignificant change during the same period (+0.5). The extent of increase in the convulsive patients was

found to be related to the degree of cerebral dysfunction as determined by delta activity on the EEG. The patients with high delta (40% or more of the sample record) had a mean increase of +8.6. Those patients with low delta indices, however, showed a statistically insignificant increase of +3.4. Following treatment the F scores were comparable to the pretreatment levels.

These findings support and elaborate previous observations on the effects of convulsive therapy. Greater agreement with the F seere scale statements during treatment show conventional stereotypy and difficulty in discrimination. The change in F score thus seem part of the same process shown by the characteristic language changes of increased denial, evasion, qualification, and use of cliches and stereotyped expressions ( ). It is also comparable to the increased difficulty in complex visual and tactile perception ( ) and figure-ground discrimination ( ).

Details of these findings were presented at the Eastern Psychological Association in 1958 and will be elaborated at the

forthcoming Divisional meeting of the American Psychiatric Association in New York.

H. Aspects of the Therapist-Patient Relationship Affecting Choice of Therapy.

As indicated previously the selection of therapy involves other aspects than the actual behavioral pattern of the patient. In the past year further efforts to clarify this problem have been undertaken, emphasizing factors in the therapist-patient relationship. We have hypothesized that such factors as increased tension, frustration and hostility in the therapist-patient relationship, as well as implicit and explicit pressures present in the environment have a significant influence in referral for somatic therapy.

In a pilot study 76 structured interviews with residents and supervisors were initiated following requests for somatotherapy. These interviews were designed to elicit the basis of the referral. It was found that in only relatively few cases was there a sudden change in the patient's clinical status which directly led to the referral. In most instances there had been

no change or progression in the presenting symptoms. Factors contributing to the timing of the referral included impending discharge, avoiding administration discharge, and pressure from the patient's family or ward personnel. It was also noted that patients with similar behavior patterns were treated differently, some given somatotherapy and others none. The reasons for this ranged from "whim" to quantitative differences in symptomatology and individual preferences for type of treatment.

The initial conclusion was that in a significant number of cases, factors other than clinical indication played a role in the referral. These same extraneous factors also influenced the timing of the referrals.

As a results of these findings a "Somatic Treatment Referral Sheet" was developed (see form at end of report) to be completed by the therapist whenever somatic therapy is requested. From this questionnaire we hope to obtain further information regarding indications for somatic treatment, more specific data

concerning the therapist-patient interaction, and a more definite idea of the therapist's expectations for such treatment.

I. Individual Differences in Selection of, and Response to Convulsive Therapy.

In the elucidation of individual differences related to somatic therapy, a variety of peripheral-cognitive procedures have been used.

The tachistoscopic perception of embedded colored figures has been given to 65 patients. The experimental group consisted of 35 consecutive referrals for convulsive therapy. The controls were 20 patients treated with phenothiazine medication (thorazine and promazine) and ten patients receiving no somatic treatment. All subjects were tested prior to treatment, and after four weeks; the convulsives were tested a third time two weeks following the cessation of treatment.

It was found that there was a statistically significant increase in mean number of errors with convulsive therapy, while following treatment there was a significant decrease from the pretreatment scores. Controls made significantly fewer errors

~~pre~~

(practice effect). There was a significant difference in errors between patients classified as showing low EEG changes (per cent time delta) when compared with high EEG changes. There were high retest correlations for all groups. Marked individual differences in response patterns were noted prior to treatment. With brain changes there was a reduction in persevaration, completion and confabulation in some patients, and and increase in others, with no unique patterns attributed to cerebral dysfunction. Even in those patients with high EEG changes, the "style" of his response pattern was ~~mtain~~ maintained. Thus a patient showing completion type errors prior to treatment would continue to make such errors with convulsive therapy, although the threshold at which completion was shown might change. Details of this study were presented at the Eastern Psychological Association in Atlantic City, April 1959.

The Rod and Frame Test (after Witkin) was administered to 47 patients consecutively referred for somatic therapy. Marked individual differences in performance were correlated with age,

education and score on the California F scale. Patients whose judgment of the vertical was strongly influenced by the surrounding frame (field dependent) were more frequently referred for convulsive therapy than drug therapy. No significant change was found with drug or convulsive treatment. For both drug/and convulsive groups retest correlations were high (.86 and .88). It is considered that individual differences on the Rod and Frame test reflect personality factors that are of importance in psychiatric treatment.

Proposal Rpt. RLK

II: 7/16/59

Altered Brain Function Following Electroshock

M-927

Progress Report - February 1, 1958 - September 1, 1959

Summary:

In our previous studies we have demonstrated that an understanding of the convulsive therapy process required a multifactorial approach involving neurophysiologic, perceptual, personality, psychodynamic and sociologic aspects of behavior. Thus it was shown that: The convulsion is essential to the therapeutic process (Fink, Green and Kahn, 1958); neurophysiologic changes reflective of altered brain function are a necessary prerequisite for behavioral change and improvement (Kahn, Fink & Weinstein, 1956; Fink & Kahn, 1957); the biochemical basis of the convulsive therapy process lay is an increased level of cholinergic activity of the central nervous system (Fink, 1958); there are characteristic perceptual changes with altered brain function induced by convulsive therapy (Fink, Kahn and Korin, 1957; Kahn and Fink, 1957); ratings of improvement after convulsive therapy are related to personality characteristics defined by Rorschach (Kahn and Fink, 1958), and family interviews (Kahn and Fink, 1957); and that evaluations of

improvement were related to changes in syntactic aspects of language (Kahn & Fink, 1958).

In the past eighteen (18) months these studies were completed and extended, and an investigation of psychopharmacologic agents begun. The framework for these investigations has been the neurophysiologic adoptive view of convulsive therapy (Weinstein & Kahn, 1955; Kahn et all, 1956; Fink and Kahn, 1957) extended to other physiodynamic treatments of psychiatric patients (Fink, 1957).

The following aspects of the convulsive therapy process were studied:

1. Significance of the Convulsion: A cooperative study of neurophysiologic, psychologic and behavioral effects of electrical and inhalant (Indoklon) induced convulsions.

2. Synaptic Basis of Neurophysiologic Change: Further studies of the effects of acute administration of experimental anticholinergic and sympathomimetric agents on both the "normal" and post-convulsive EEG.

3. Sociopsychologic Aspects of Convulsive Therapy:

a. Relation of the factors of age, education, nativity and

stereotypy (measured by the California F scale) with selection of therapy, duration of hospitalization, diagnosis and discharge ratings.

b. Changes of F scale with treatment, and relation of these changes to EEG indices.

4. Psychotherapy and Convulsive Therapy:

In supervisory sessions, alterations in psychotherapy with convulsive therapy were studied.

5. Perception:

Both patterns of change and individual differences on tachistoscopic figure/ground discrimination tasks, critical flicker frequency and perception of the upright with induced convulsions were studied.

These studies were extended to drug therapies and the following studies undertaken:

1. Neurophysiologic:

a. Relation of EEG change on acute and chronic administration of psychopharmaceuticals to clinical behavioral change.

b. EEG as a screening device for psychopharmaceutic potency.

c. Relation of EEG changes to hallucinogenic activity.

d. EEG effects of megimide.

2. Communication Patterns:

Relation of induced neurophysologic change to dyadic diversification and syntactic language measures.

3. Aspects of the Therapist - Patient Relationship affecting choice of somatic therapy.

These studies have supported and expanded the neurophysiologic-adaptive view of convulsive therapy, and demonstrated that such a hypothesis has applicability to our understanding of the mode of action of psychopharmacologic agents.

PROGRESS REPORT:

A. THE CONVULSIVE THERAPY PROCESS

1. Significance of the Convulsion:

A comparable study of Indoklon and electrically-induced convulsions in psychiatric therapy was completed. An earlier convulsive-subconvulsive control study demonstrated that significant behavioral changes occurred almost exclusively in patients receiving grand mal electroconvulsive therapy. The present report is an assessment of

the relative neurophysiologic, behavioral and clinical effects of two different methods of inducing convulsions - electrical (alternating current) and inhalent (indoklon).

Twenty-five consecutive patients referred for convulsive therapy were randomly classified into two groups - seizures induced in thirteen patients by the standard Medcraft alternating current instrument, and in twelve by the inhalation of hexafluorodiethyl-ether (indoklon). In both groups treatment was administered three times a week for a total of 10 to 24 applications, determined on the basis of clinical criteria by the supervising psychiatrist.

All patients were tested one to two days prior to the first treatment, following 10-12 treatments, and two weeks following the last treatment. In addition to evaluations of behavioral change, tests included measures of intellectual function (five subtests from the Wechsler-Bellevue Intelligence Scale), perception (figure-ground discrimination using embedded geometric figures, the perception of pseuoisochromatic color plates at high speeds of tachistoscopic exposure, and the Street incomplete figures test), and social

attitude (the Levinson revision of the California F Scale). An electroencephalogram was obtained during each of the testing periods, and measured for the per cent time slow wave (6 cps or slower) activity from a continuous 66 second sample.

The results failed to show any significant intergroup test differences between the electroshock and indoklon groups at each of the three test periods.

Intragroup analysis, however, showed that during treatment both groups made increased errors on the intellectual and perceptual tests, and had higher scores on the F scale. By two weeks after the termination of treatment both groups returned to near pretreatment levels for most tests.

Both groups were comparable for the degree of induceed EEG slow wave activity after 10-12 treatments. The per cent time slow activity for the indoklon group was 51% and for the electroshock group 47.5%. Within each group individual differences in behavioral change were related to the degree of neurophysiologic change - those with the highest per cent time delta showing the greatest behavioral change.

Rank order correlations between changes in test performance and degree of slow wave activity with treatment were positive for all procedures, except the comprehension subtest of the Wechsler-Bellevue, and reached a level of statistical significance for digit span (+ .61, p .01), object Assembly (+.46, p .05), F scale (+ .38, p .05), tachistoscopic perception (+.67, p .01) and perception of embedded figures (+.43, p .05).

This study demonstrated that two different convulsant agents produce similar neurophysiologic and behavioral changes. It was concluded that the behavioral change in convulsive therapy is related to the degree of altered brain function, and are non-specific for the type of agent used to induce the convulsion.

(Presented, in part, at the Eastern Psychological Assocation, Atlantic City, April, 1959).

2. Biochemical Aspects of the Convulsive Therapy Process.

The significance of high voltage EEG delta activity in the convulsive therapy process (Roth et al, 1951, 1957; Fink and Kahn, 1957) and the report that this delta activity was blocked by the administration of the anticholinergic agents atropine and scopolamine (Ulett and Johnson, 1957) provided the basis for these studies. As

there were attendant unpleasant systemic effects with the administration of these agents, reports describing diethazine as an anticholinergic compound with potent neurologic but minimal systemic effects (Jenkner and Lechner, 1955; Lechner, 1956) let us to undertake studies similar to those of Ulett and Johnson using this compound (Fink, 1958). These observations with diethazine let to the investigation of other experimental anticholinergic agents.

Clinical and electroencephalographic responses to the intravenous administration of diethazine Win. 2299, benactyzme, JB 318, JB 336 and atropine in psychiatric patients at various stages of convulsive therapy were studied. Each is a potent anticholinergic agent <u>in vitro</u>.

The subjects were ninety psychiatric patients referred for convulsive therapy, ranging in age from 18 to 67, with a variety of diagnoses. A total of 107 observations were made, since some subjects were studied with more than one compound.

The observations were made in the EEG laboratory using a standard 8 channel instrument and needle electrodes. In each trial, the compound under study was administered intravenously at a set rate

per minute until clinical behavioral or electrographic changes were observed.

It was observed that administration of these anticholinergic agents was associated with a) desynchronization of EEG rhythms with a blocking of post-convulsive delta activity; b) alerting, excitatory behavioral response with illusory, delusional and hallucinatory ideation, and c) systemic effects of muscular weakness, dryness of the mouth, dry skin and tachycardia. The electrographic, behavioral and systemic effects were concurrent.

These observations are regarded as consistent with the suggestion that the physiologic basis of convulsive therapy lies in an increase in central nervous system cholinergic activity.

Observations that LSD, amphetamine, mescaline and diphenhydramine - sympathomimetic and antihistaminic agents - also induced EEG desynchronization, blocking of post convulsive delta activity and clinical excitatory activity support the suggestion that the behavioral and electrographic patterns of these compounds are also based on alteration in synaptic activity. Increased synaptic activity (cholinergic, sympatholytic effects) is associated with EEG hyper-synchronization, and clinical sedation and euphoria; while decreased

synaptic activity (anticholinergic, sympathomimetric) is associated with EEG desynchronization and clinical excitatory and hallucinogenic states, thus supporting the hypothesis initially described by Wikler (1954).

Descrepant observations with the anticholinergic agent, atropine, are considered to be related to significant differences in dosage.

(Presented, in part, at the Society of Biological Psychiatry, San Francisco, 1958 and awarded the first A. E. Bennett Psychiatric Research Award of that Society; and, in part, at American EEG Society, Atlantic City, 1959. Published, in part, A.M. A. Arch. Neurol. & Psychiat. 80: 380-387, 1957; and accepted for publication, EEG Clin. Neurophyscol.)

3. Sociopsychological Aspects of Psychiatric Treatment.

a. Duration of Hospitalization, Diagnosis and Discharge Evaluation.

In an earlier study of the Hillside Hospital population(Kahn, Pollack & Fink, 1957), it was noted that age, education, place of birth and social attitudes as measured by the California F scale, were related to the selection of therapy. Those patients who were older, had less education, were foreign-born and with high stereotype scores on the F scales were more likely to receive convulsive therapy.

In contrast, patients who were younger, better educated, native-born and obtained low scores on the F scale, received psychotherapy as their sole form of treatment.

Ancther study was undertaken to determine the relations of these sociopsychological factors to 1) the duration of hospitalization, 2) the clinical evaluations at time of discharge, and 3) the final diagnosis.

The entire in-patient adult population on March 7, 1957 was studied. This consisted of 171 patients, 57 men and 114 women, ranging in age from 16 to 68 years, with a median of 35 years.

Patients hospitalized for the shortest period (1 - 5 months) were noted to be the oldest, have the least education, were more likely to be foreign-born, and have the highest scores on the F scale. Younger, native-born, more educated, lower F score patients were hospitalized the longest (10 or more months). The same relationship of these factors to length of hospitalization was found when separate analyses were made according to diagnosis and type of treatment (convulsive therapy or psychotherapy).

Discharge evaluations of improvement were significantly related to age - the older patients having the most favorable ratings. Analysis of the data by type of treatment, however, demonstrated that among the convulsive therapy patients ratings of recovered or much improved were given to those patients with the highest F scores, least education and who were foreign-born.

Diagnoses of schizophrenia or psychoneurosis were associated with lower F scores, younger ages, more education and native birth. The older, less educated, foreign-born, high F score patients were more frequently classified as involutional or manic-depressive psychosis.

It was postulated that these relationships reflect the influence of social background and psychological processes, such as the behavioral patterns of communication and modes of expression. These These not only contribute to the pattern of mental illness, but affect all aspects of the patient-therapist interaction.

(Presented at the Eastern Psychological Association, Atlantic City, April, 1959, and the Academy of Psychoanalysis, Philadelphia, April, 1959. Accepted for publication, Archives of General Psychiatry.)

b. Changes in Social Attitude with Convulsive Treatment.

Following the earlier observations that the California F scale is useful in understanding referral for convulsive therapy and the evaluation of clinical response following such treatment, further studies were undertaken with thisscale in regard to the following questions: 1) What does the F scale measure in a psychiatric population? 2) Do F scores change with convulsive therapy? 3) Are these changes related to the degree of altered brain function?

The entire in-patient population of the hospital was given the F scale, and one month later, was retested with a "reverse" F scale, in which each statement was changed to the opposite of the original. The "reverse" scale was scored in the same manner as the conventional scale, with high scores reflecting greater agreement.

It was noted that those patients who made low scores initially, indicating a predominant disagreement with the statements, showed an increase on the "reverse" scale, indicating a high degree of agreement. In contrast, patients who made high scores initially showed little change on retesting, agreeing with the statements to the same

extent even though the meaning was reversed. It is evident that low F score patients are more critical and discriminating persons, while those with high F scores are more undifferentiating and stereotyped in their reactions.

This observation is related to the process of selection of patients for convulsive therapy. A high degree of sterotypy of thinking and communication is incompatable with the establishment of a conventional psychotherapeutic relationship, preventing the psychoanalytically-oriented psychotherapy stressed at Hillside Hospital. It follows that the high F score patients will be unsuccessful in psychotherapy and most likely referred for convulsive therapy.

In another study, sixty-nine patients were given the F scale before, during (at 10-12 treatment period) and after convulsive therapy. Ten patients, selected at random, constituted a control group and received subconvulsive electrostimulation. There was a mean increase in F score of +5.7 during treatment in convulsive group - a difference significant at the 5% level. In contrast, the

In contrast, the control group showed an insignificant change during the same period (+0.5). The extent of increase in the convulsive patients was related to the degree of cerebral dysfunction as determined by delta activity on the EEG. The patients with high delta (40% or more of the sample record) had a mean increase of +8.6. Those patients with low delta indices, however, showed an increase of +3.4. Following treatment the F scores were comparable to the pretreatment levels.

These findings support and elaborate previous observations on the effects of convulsive therapy. Greater agreement with the F scale statements during treatment show conventional stereotypy and difficulty in discrimination. Changes in F score thus parallel the characteristic language changes of increased denial, evasion, qualification, and use of cliches and stereotyped expressions (Kahn & Fink, 1958). It is also comparable to the increased difficulty in complex visual and tactile perception (Fink, Kahn & Korin, 1957) and figure-ground discrimination (Kahn & Fink, 1957).

(Presented at the Eastern Psychological Association, 1958; and accepted for presentation at the Divisional Meeting of the American Psychiatric Association, New York, November 1959.)

4. Psychotherapy and Physiodynamic Therapy:

Previous studies indicated that patients referred for electroshock in this hospital are of two types. The largest number are patients in the older age groups who have limited education and are foreign born. They tend to be non-introspective persons, stereotyped in their language and thinking and verbally uncommunicative. Their predominant symptoms are depression, agitation, withdrawal and somatization. The second, and smaller, group of patients are younger, native-born, better-educated, and verbally communicative with a capacity for introspection. They characteristically exhibit thinking disorders and overactive behavior, with lesser degrees of somatization and depression.

Four patients, two for each group described above were studied to determine 1) reasons for referral, 2) whether different attitudes were required in psychotherapeutic management, and 3) the relation of the psychotherapeutic

approach to the patient's clinical response to convulsive therapy.

It was suggested that these patients were referred for convulsive therapy because of a failure of communication in the psychotherapeutic relationship. In two cases this was a reflection of the patient's limited verbal and introspective capacity related to educational and social factors. In two instances, however, the impaired communication was manifested by unmanageable acting out behavior.

Following treatment, the older, less educated patients were able to maintain a behavioral change with a reassuring, supportive technique, amplifying tendencies to minimization and denial developed during electroshock. In the better educated patients, electroshock decreased acting out was associated with increased use of interpretive forms of psychotherapy.

It was concluded that the relationship of psychotherapy to convulsive therapy varies with the communication pattern

and adaptation shown by the individual patient. (Published in the Journal of Hillside Hospital, 7: 17-25, 1958).

5. Perception:

A variety of perceptual-cognitive test procedures have been stumied in patients receiving somatic therapies.

1. The Tachistoscopic Perception of Embedded Colored Figures:

This task was studied in an experimental group consisting of 35 consecutive referrals for convulsive therapy, and "control" groups of 20 patients treated with phenothiazine medication (thorazine and promazine) and ten patients receiving no somatic treatment, matched for age. All subjects were tested prior to treatment, and after four weeks the convulsive patients were tested a third time two weeks following the cessation of treatment.

There was a statistically significant increase in mean number of errors with convulsive therapy, and following treatment, there was a significant decrease from the pretreatment scores. "Control" subjects made significantly fewer errors (practice

effect). There was a significant difference in errors between patients classified as showing low EEG changes (per cent time delta) when compared with high EEG changes. There were high retest correlations for all groups.

There were marked individual differences in response patterns prior to treatment. With brain changes there was a reduction in perseveration, completion and confabulation in some patients, and an increase in others, with no unique patterns attributed to cerebral dysfunction. Even in those patients with high EEG changes, the "style" of his response pattern was maintained. Thus a patient showing completion type errors prior to treatment would continue to make such errors with convulsive therapy, although the threshold at which completion was shown might change. Details of this study were presented at the Eastern Psychological Association in Atlantic City, April 1959.

2. Rod and Frame Test (Witkin): This task was administered to 47 patients consecutively referred for somatic therapy. Marked

individual differences in performance were correlated with age, education and score on the California F.scale. Patients whose judgment of the vertical was strongly influenced by the surrounding frame (field dependent) were more frequently referred for convulsive therapy than drug therapy. No significant change was found with drug or convulsive treatment. For both drug and convulsive groups retest correlations were high (+.86 and +.88). It is considered that individual differences on the Rod and Frame test reflect personality factors that are of importance in psychiatric treatment.

B. PSYCHOPHARMACOLOGIC STUDIES

1. Neurophysiologic Studies:

Accprding to the neurophysiologic-adaptive view of the convulsive therapy process, the clinical efficacy of repeated induced convulsions is dependent upon the induction of a persistent alteration in central nervous function, providing a milieu for changes in the subject's interaction with the examiner and the environment. In these studies the best index of neurophysiologic change has been those aspects of cerebral function reflected by delta activity in the electro-

encephalogram (Fink and Kahn, 1957).

The efficacy of newer psychopharmaceuticals in altering psychotic behavior patterns has led to the suggestion of a similar hypothesis for the mode of action of these agents, and to studies of the relationship and specificity of altered behavioral patterns to neurophysiologic change as reflected in electroencephalography.

Of the psychopharmaceuticals tested in acute experiments an increase in synchrony with or without an increase in slow wave activity has been observed for chlorpromazine, promazine and trifluprομazine. Behaviorally, these drugs were associated with a) increasing sedation, drowsiness, denial and euphoria; b) decreasing agitation, panic, excitement and delusional and hallucinatory activity; and c) minimization and displacement of symptons. Barbiturates regularly induced an increase in fast activity with an increase in synchrony, with the associated behavorial changes of sedation, euphoria, denial and minimization. Amphetamine and methamphetamine increased fast activity without increased synchrony and behaviorally were associated with behavorial alerting, hypomania,

excitement and increased motor activity. Decrease in voltage and per cent time of slow wave activity in subjects with post-convulsive delta activity was seen with LSD-25, benactyzine, Win-2299, JB-318, JB-336 and diethazine. Of these drugs, benactyzine produced increased alerting, excitement, tension and panic; the other drugs also produced illusory sensations and hallucinatory, delusional and paranoid ideation.

The electrographic patterns were consistently altered concurrently with behavioral changes both in the acute and chronic administration studies. Tranquilization, euphoria, sedation and minimization of symptoms were concurrently associated with increased EEG synchronization and shift of frequencies to the delta range. Agitation, tension, panic, excitement, illusions and hallucinations were associated with desynchronization of frequencies.

Similar patterns were demonstrated in subjects with prior delta activity. Agents that tended to synchronize frequencies, as chlorpromazine and barbiturates, augmented the per cent time delta activity and enhanced the clinical patterns; agents that desynchronized frequencies, as diethazine, LSD-25

and benactyzine, minimized the clinical effects typically ascribed to repeated convulsions.

Various experimental psychopharmaceuticals were tested. In addition to extensive studies of B-B methylethylglutarimide (Megimide) and hexafluorodiethylether (Indoklon) the following agents were studied: phenyltoloxamine (PRD-Bristol), methonalide (BLM-188, Bristol), tropin-4-Chlorbenzhydryl ether (WY-2149, Wyeth), dimethylaminoethanel and its congeners (Deaner and varieties, Riker), JB-318, 329 and 336 (various piperidyl-benzilates, Lakeside) and imipramine (Tofrānil, Geigy).

Because of ~~xixgi~~ significant behavioral and electrographic changes, a more intensive investigation of imipramine (Tofrānil), was undertaken. In 28 acute experiments, consecutive patients referred for physiodynamic therapies were tested in the EEG laboratory at various stages of treatment. Tofrānil solution (10 mg/cc) was administered intravenously at a set rate (1 cc/40 sec) until electrographic or behavioral changes became prominent, for a total of 40-125 mg (0.5-2.5 mg/kg). Behavioral observation

and electrographic recording continued for one to three hours. In patients referred for pharmacotherapy because of manifest depressive, withdrawn or retarded behavior oral Tofrānil of 75-350 mg was administered.

In the acute studies there was initial restlessness, associated with dizziness, dry mouth, "faintness," nausea, and on four occasions, vomiting. These symptoms persisted for 10-20 minutes, and were accompanied by lassitude, heaviness of the extremities and eventual drowsiness. Heart rate was unchanged or slowed. Blood pressure dropped by 20-40% in older (age > 60) patients. Subsequently, subjects were relaxed, quiet and disinclined to activity, even when returned to their ward.

The electrographic patterns accompanying these behavioral changes were initiated by a gradual decrease in voltages during the injection. By ten minutes, the per cent time alpha had been halved. In patients with moderate amounts of beta activity, such activity occasionally increased in voltage and

per cent time. By twenty minutes, in association with behavioral lassitude, low voltage (to 50 microvolts) random theta frequencies (5-7 cps) appeared. In records with post-convulsive delta activity, there was a marked decrease in voltage and per cent time of slow wave activity. These electrographic patterns persisted for ½ to two hours.

There was considerable individual variability in this acute EEG response. In patients who received 100 mg or more of Tofrānil, EEG and behavioral changes were observed in all but three. In six patients, dosage of Tofrānil less than 50 mg were associated neither with EEG nor with behavioral changes.

In chronic Tofrānil studies, behavioral changes generally appeared during the second, and were maximal during the third, week of treatment. The most prominent behavioral adaptation was euphoric denial. Patients complained less of somatic symptoms, and denied, minimized or displaced their illness on inquiry. It became increasingly difficult to discuss significant life relationships with them. In six patients somatization and

restlessness increased and depressive affect persisted. In three, restlessness, agitation, excitement, insomnia and vomiting, led to the cessation of therapy. No change in symptoms were noted in five patients after four weeks of therapy.

Electrographic studies on chronic administration showed a decrease in voltages with poorer record modulation. Low voltage theta (5-7 cps) activity up to 10% appeared. Well defined fast activity became more prominent in a few.

(Presented at the Collegium Interantionale Neuro-Psychopharmacologicum, Rome, September, 1958; at the Conference on Depression and Allied States, Montreal, March, 1959; and American EEG Society, June, 1959. Published, in part, in the Proceedings of C.I.N.P. Psychopharmacology Frontiers, ed. N. Kline, 325-332, 1959; Canad. J. Psychiat., 1959 (in press); Neurology, 8: 682-685, 1958.

2. Language Patterns as Measures of Behavioral and Neurophysiologic Change with Drugs.

In previous studies of the convulsive therapy process, it was demonstrated that two language measures, a syntactic content analysis (Kahn and Fink, 1958) and dyadic diversification scores of instructured interviews (Jaffe, Kahn and Fink, 1958) provided objective indices of behavioral change, and were related to the degree of altered brain function. In a further test of these language measures as indices of behavioral and neurophysiologic change, they were applied to interview on acute administration of various psychopharmacologic agents.

Seventy-two interviews with patients at various stages of drug therapy have been analyzed, using the following agents: amobarbital, benactyzine, chlorpromazine, diethazine, lysergic-acid diethylamide, and Win-2299.

Following a routine electrographic recording, an unstructured psychiatric interview, with short periods of structured inquiry, was tape recorded. With EEG running, an intravenous injection was then given at a slow rate. When

specific electrographic or clinical changes were induced, the interview was repeated. Recording periods of EEG and verbal behavior were alternated for the duration of the observation period. The EEG was measured for changes in synchronization, shifts in dominant frequencies, and per cent time of slow waves (delta) and beta frequencies.

The tape recordings were transcribed and measured for the diversification of consecutive 25 word samples of speech of both participants (dyadic) and for syntactical changes. In the dyadic analysis, the pooled verbal behavior of both participants was transcribed, divided into 25 word samples, and for each sample the ratio of the number of different words to the total number of words (a diversification score) was calculated. The syntactic langu ge mnalyses were based on the response to standardized questions using a method previously described (Kahn and Fink, 1958), scoring such changes as syntactical use of person, alteration in tense, evasion, qualification, displacement or verbal denial of symptoms, use of stereotyped expression or cliches, cryptic

response, and withdrawal or silence.

Consistent changes were observed in both the dyadic diversification and syntactic language measures in subjects classified according to the neurophysiologic and behavioral effects of the drugs applied.

Amobarbital and chlorpromazine are neurophysiologic synchronizing agents. Amobarbital regularly inducing high voltage well synchronized fast activity at 20-24 cps, while chlorpromazine administration was followdd by increased synchronization of the EEG record and a shift to slower frequencies including occasional slow wave burst activity. Behaviorally these drugs are associated with sedation and tranquilization. On the language measures there was an increase in stereotpy and repetitiveness associated with increasing use of clichés, alterations in tense, displacement and evasion.

Diethazine, benactyzine, LSD-25 and Win-2299 are neuro-physiologic desynchronizing compounds. These drugs are characteristically associated with decreased voltage and per

cent time of alpha activity and increased irregular low voltage fast activity. Behaviorally hallucinatory, excitatory or illusory activity are observed. On the language measures there was decreasing repetitiveness, wide diversity of words, less variability of diversification scores, and decreased use of clichés and alterations in tense.

Further explanation of language measures are suggested as a rational basis for the understanding of the psychologic effects of the new therapies.

(Presented at the Conference on Psychodynamic, Psychoanalytic and Sociologic Aspects of the Neuroleptic Drugs in Psychiatry, Montreal, April, 1958, and at the American Psychiatric Association, Philadelphia, April, 1959. To be published).

3. Aspects of the Therapist-Patient Relationship Affed ting Choice of Therapy.

The selection of therapy involves aspects other than the manifest behavioral patterns of the patient. In the past year further efforts to clarify this problem have been undertaken, emphasizing factors in the therapist-patient relationship. We

have hypothesized that frustration and hostility in the therapist-patient relationship and implicit or explicit environmental pressures have a significant influence in referral for somatic therapy.

In a pilot study 76 structured interviews with residents and supervisors were initiated following requests for somatotherapy. These interviews were designed to elicit the basis of the referral. It was found that in only relatively few cases was there a sudden change in the patient's clinical status which directly led to the referral. In most instances there had been no change or progression in the presenting symptoms. Factors contributing to the timing of the referral included impending discharge, avoiding administrative discharge, and pressure from the patient's family or ward personnel. It was also noted that patients with similar behavior patterns were treated differently, some given somatotherapy and others none. The reasons for this ranged from "whim" to quantitative differences in symtomatology and individual preferences for type of treatment.

It was concluded that factors other than clinical indication played a role in the referral in a significant number of cases. These same extraneous factors also influenced the timing of the referrals.

As a result of these findings a "Somatic Treatment Referral Sheet" was developed (see form at end of report) to be completed by the therapist whenever somatic therapy is requested. From this questionnaire and continued therapist and ward personnel interviews we hope to obtain further information regarding indications for somatic treatment, more specific data concerning the therapist-patient interaction, and a more definite idea of the therapist's expectations for such treatment.

September 1, 1959

FINAL REPORT

M-927*

Department of Experimental Psychiatry

HILLSIDE HOSPITAL
Glen Oaks, L. I., N. Y.

1. Acknowledgment a.
2. Summary, Five Years, 1954 - 1959 b.
3. Summary #4, Feb. 1, 1958 - Sept. 1, 1959
4. Publications, 1954 - 1959 25
5. Presentations, 1954 - 1959 30

* Initial studies begun Fall 1953, supported by the Board of Directors' Research Fund. Supported by National Institute of Mental Health Fund, September 1, 1954 - August 31, 1959. Study continuing with support of grant MY-2715, United States Public Health Service (Jan. 1, 1959)

Acknowledgment

The studies reported here would not have been possible without the faith and support of the Founder of Hillside Hospital, Dr. Israel Strauss, the Board of Directors and the Administrator, Mr. Maurice Bachrach, who sustained this program during its early vicissitudes.

Financial Support was also given during this period by the Kaufman Foundation, the Foundations' Fund for Research in Psychiatry, the Dazian Foundation of New York; the following pharmaceutical firms: Smith, Kline and French Laboratories, Wyeth Laboratories, Geigy Pharmaceuticals, and Bristol Laboratories; and the Mental Health Board of Nassau County.

SUMMARY

M - 927

1954 - 1959

The laboratories of the Department of Experimental Psychiatry were established at Hillside Hospital in September, 1954. During this five year period neurophysiologic, psychologic (personality and perceptual), lingustic, and sociologic aspects of "somatic" psychiatric therapies have been the principal foci.

1. Convulsive Therapy:

The view of the convulsive therapy process as the induction of a non-specific state of altered brain function, similar to craniocerebral trauma (10, 11, 21) was supported and amplified with this altered cerebral milieu, subjects were seen to respond in various ways (26) of which the most successful was explicity verbal denial (7, 31). This latter was most prominent in characterologically disposed individuals (36).

An alteration in brain function was pre-requisite to behavioral change (7, 8, 11, 26). Grand mal seizures were essential to this process (26) but electrical induction was not (B-42). Such alteration in brain function was measured by various ways including electroencephalography (6, 11, 12, 24, 39, language patterns (4, 7, 14, 31, 43, B-24), perceptual tasks (2, 16, 17, 37, 46, B-26, 41, 42) and tests of recall.

A variety of behavioral changes were seen during convulsive therapy (26, B-17). Such patterns were viewed as adaptations to altered brain function, and were believed dependent upon

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Reference numbers are to publications or presentations (B-) listed in the appendix.

characterologic and environmental factors (7, 25, 26, 36, 40). Clinical ratings of improvement were seen as value judgments by the observer of the behavioral changes in the subject (26). Adaptations characterized by denial mechanisms, both in behavior (B-17) and in language (7, 31) were assessed with the best rating of improvement. Such adaptations were noted to be related to habitual modes of conduct (character, personality) (36, B-11, 32).

The durability of the altered behavioral modes was seen to be dependent upon such factors as the degree and duration of altered brain function, the environmental expectations, and the type and degree of family and medical support. Different behavioral patterns were best supported by varying types of psychotherapy (19).

It was also suggested that the neurophysiologic basis of convulsive therapy may lie in an alteration in central synaptic cholinergic - adrenergic relationships, with a predominant shift to increased cholinergic activity as the operationally significant pattern. Such interpretations were based on the relationship of high voltage EEG slow wave activity to behavioral change (6, 11, 26) and the blocking of the electrographic and behavioral changes in central anticholinergic agents (21, 34, 35, 41, 42) and by central sympathomimetics (42).

Measures of linguistic behavior in structured (7, 31) and unstructured (14, 29, B-24) interviews showed characteristic

alterations towards increased denial, minimization, displacement, stereotypy and repetitiveness, related to the degree of altered brain function (B-24). These changes were blocked or reversed by anticholinergic hallucinogens (21, 43).

Various perceptual tasks provided indices of behavioral change and were related to the degree of altered brain function. These included the perception of simultaneous tactile stimuli (17), embedded (Gottschaldt) figures (37, B-16), and tachistoscopically exposed words (37) and embedded color figures (41).

Sociopsychologic aspects of age, years of education, nativity and degree of stereotypy and conventionality (measured by California F Scale) were also studied and were related to selection of therapy, duration of hospitalization, diognosis and treatment response/ in hospitalized patients (15, 36, 40, 45).

2. Neurophysiologic-Adaptive Hypothesis of Somatic Therapy.

Based on these studies, a hypothesis of the mode of action of other psychiatric therapies such as insulin coma, leucotomy and psychotropic drugs, was expressed (10, 33, 38). This view holds that these therapies are also methods of inducing varying states of altered brain function, in which varying adaptive patterns may become prominent. The adaptive pattern is viewed as dependent upon the type, degree and duration of altered brain function, the personality of the subject, and tolerances and expectations of the environment.

Examination of this hypothesis as applied to drug therapies is now in progress, supported by USPHS grants MY-2092 and MY-2715.

3. Insulin Coma Therapy.

An initial case description (3) showed the significance of denial patterns and persistent altered brain function to the behavioral change in this form of therapy.

In an insulin coma - chlorpromazine control study (27), no differences in hospital improvement ratings were observed in the two treatment groups. Chlorpromazine was safer, easier to administer, permitted continued administration and allowed for greater degrees of concurrent relationship therapy than insulin coma. These observations led to a replacement of insulin coma by psychotropic drugs in this institution.

4. Pharmacotherapy.

Also derived from these hypotheses is the ongoing program in evaluating various psychopharmaceuticals. Electrographic and linguistic analyses of effects of acute introvenous administration and chronic clinical administration of various new compounds are in progress. EEG patterns, along such continua as synchronization-desynchronization, and frequency shift are being related to behavioral (21, 34, 41, 42) and linguistic changes (21, 43).

The neurophysiologic basis of experimentally induced hallucinogenic states have also been interpreted as an alteration in synaptic chemical relations, such that the effective levels of cholinergic activity is decreased (42). Initial work on this hypothesis ( ) is now being expanded.

In addition to these phenomena, other patterns of language and non-verbal aspects of behavior have been observed which can also be understood as symbolic forms of adaptation to illness. These include the syntactical use of the second and third person, changes in mood, withdrawal and selective inattention, and alterations in sexual behavior (6).

These types of behavior have been observed in enduring fashion in patients whose lesions and electroencephalographic records indicated diffuse cerebral dysfunction. In patients with brain damage who did not show delusional denial and disorientation on ordinary clinical examination, the phenomena might be elicited in an interview following the intravenous administration of amytal sodium. This observation furnished the basis for the "amytal test" for brain disease in which the persistence of certain patterns of denial and disorientation is considered an indication of cerebral dysfunction (4,5).

In considering further the relationship between brain damage and the mechanism of denial it has been demonstrated that the premorbid personality was important in determining what type of symbolic adaptation occurred. Thus, patients with the most striking and enduring manifestations of anosognosia were those who had habitually used verbal denial and rationalization as a means of coping with their problems (10).

On the basis of these observations the hypothesis was developed that the therapeutic action of electrically induced convulsions lay in the creation of a milieu of brain function in which the patient might express his problems in symbolic fashion, particularly in the form of explicitly denying them. A case was reported in which a patient received electroshock treatment in an attempt to relieve intractable pain associated with a spinal cord tumor (11). After a number of treatments, coincident with the appearance of disorientation for a place and time, paraphasic misnaming and a euphoric state, the patient denied pain. When these associated phenomena were not clinically apparent they