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PREDICTION OF INDIVIDUAL PATIENT RESPONSE TO CONVULSIVE THERAPY 1

Max Fink, M. D.

The prediction of response to treatment is a necessary daily task of medical practitioners, who, after a process of clustering the symptoms and signs of illness of a patient, select a treatment regimen most likely to effect a salutary change in the patient. Where the classification of the disease is established by definitive criteria as in syphilis, diabetes or malaria - the physician's problem is simplified. Where classification is not based on definitive criteria, as in heart disease, or mental disease - the physician's problem is complex, for he must resort to the recognition of pattern based on his individual experience. Such classification is not readily validated, and in the absence of specified external criteria, errors in grouping for therapeutic purposes are frequent.

In the instances where remedies are established by their effectiveness, as in syphilis, or bacterial infections, or avitaminosis - treatment selection is readily defined. Where remedies are non-specific, as in the treatment of mental illness by environmental manipulation, psychotherapy and various physiodynamic therapies, the problem is complicated, not only by the non-specificity of treatment but by the probability that potentially effective therapies are applied to potentially responding and potentially nonresponding populations.

The problem is further complicated by a lack of evaluative criteria of salutary change. Various approximations are in use, as symptom rating scales, social adaptational measures, patient self-ratings, and changes in target symptoms. These indices are generally too broad, too inclusive and too non-specific to be useful. For example, in the target symptom approach, the assumption that anxiety in neurotic phobic, neurotic depressed, or paranoid schizophrenic subjects are equivalent processes is not valid. Depression in various subjects is no more the same phenomenon than is the fever in tuberculosis, pneumonia or lung abscess.

There are, therefore, three aspects to the problem of predicting individual patient response to therapy: the specification of populations (patient selection); the selection of therapy; and the specification and evaluation of behavioral change. These aspects will be described with reference to the convulsive therapy evaluation programs of the Hillside Hospital as studied during the past seven years. Hillside Hospital is a voluntary, non-profit, community supported institution in New York City. In these studies, the patients were referred specifically for convulsive therapy by staff psychiatrists to the special somatic treatment unit which was responsible for all somatic treatments at the hospital.

Methods

Since treatment selection was defined by the institution, our studies initially focused on the definition of parameters of change.

Observing the usual mixed group of subjects referred for convulsive therapy, we recorded a variety of behavioral adaptive patterns at the times when subjects had received the number of treatments sufficient to induce neurophysiological changes. The patterns included euphoria, hypomania, denial, and minimization; memory loss and increased complaining; increased fearfulness, agitation and excitement; and withdrawal, paranoid and delusional ideation. In assessing these patterns, that of euphoria, hypomania, denial and minimization was prominently associated with clinical ratings of much improved and recovered. We termed this adaptive mode "euphoric-hypomanic" and set this as the criteria for the behavioral change which we would like to predict (1).

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

Aided, in part, by grants M-927 and MY-2715 of the National Institute of Mental Health, U. S. Public Health Service.

To determine the population prone to show this adaptive pattern (and therefore be rated as much improved and recovered) we eschewed the usual diagnostic terms or symptom check list, and sought more measurable aspects of behavior. During these studies we had developed a concept of the convulsive-therapy process which we termed the neuro-physiologic-adaptive view (2). In this view, repeated convulsions are seen as a device to alter brain function. Under the conditions of such altered brain function behavioral adaptations emerge based on individual personality, sociocultural and attitudinal factors. Thus, we sought measures of pre-treatment personality and attitude as predictive indices.

For the most part, it was after we had completed these studies that we defined the "euphoric-denial" pattern, so that on these tables the earlier clinical ratings of "much improved" and "recovered" are reported and are, in our view, to be equated with this behavioral pattern.

Results

a. Language measures. Our first assessment was of language patterns. Earlier studies by Weinstein and Kahn (3) had demonstrated that patients with brain dysfunction had characteristic language changes of denial, disorientation and confabulation after intravenous amobarbital. In one electroshock study we observed that these same language changes occurred with increasing numbers of treatments. We also noted that those patients showing these language changes were the ones evaluated as recovered, while those not exhibiting the changes were generally rated as unimproved. A linguistic content analysis showed the language patterns rated in the study to be explicit denial, minimization, displacement, evasion, cliches, cryptic comments, use of third person, change of tense, withdrawal, qualification, and responding with a question (4).

It seemed probable that the subjects who showed these language patterns after electroshock would be the ones who have a propensity to using such patterns before treatment - if we could elicit the language changes by some provocative test. We, therefore, tested each patient before electroshock by asking questions in a short structured interview, administered amobarbital until there was slurred speech and nystagmus, and then repeated the questions (3). We scored the answers for the number of language changes after amobarbital (4).

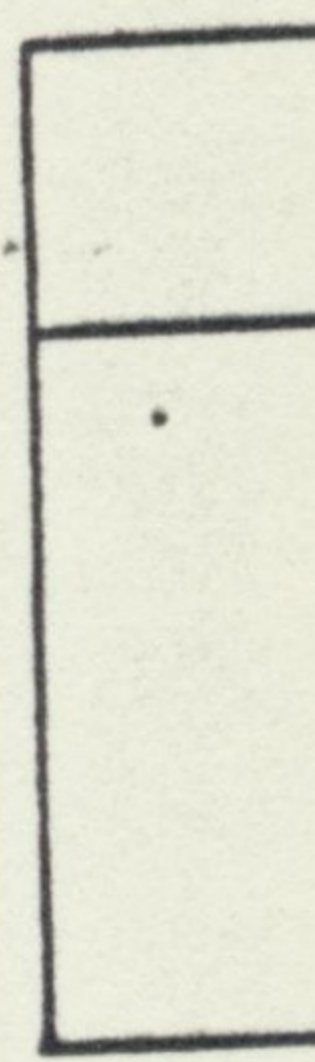
We noted a relation between the number of pretreatment language pattern changes following amobarbital to the number of language changes manifested clinically during the fourth week of treatment (Table 1). Furthermore, there was also a relationship between the number of pre-treatment language changes and short term clinical ratings of much improved and recovered (Table 2).

TABLE 1
RELATION BETWEEN PRETREATMENT LANGUAGE RESPONSE TO AMOBARBITAL SODIUM AND CLINICAL CHANGES AND WITHDRAWAL DURING TREATMENT

Subject	No.	Three or more clinical language patterns*	Withdrawal reactions to amobarbital sodium:
Pretreatment response to amobarbital sodium	30	18 60%	21 70%
No pretreatment response to amobarbital sodium	35	11 31%	12 34%

* $X^2 = 4.26; p < .05.$
+ $X^2 = 6.88; p < .01.$

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TABLE 2

RELATION OF PRETREATMENT LANGUAGE CHANGES WITH AMOBARBITAL SODIUM TO EVENTUAL CLINICAL RESPONSE

Change	No.	Change with amobarbital sodium*	
Much Improved	28	19	68%
Moderately Improved	22	8	36%
Unimproved	15	3	20%

* $\chi^2 = 10.30$; $P < .01$

b. Family Interviews. Our second assessment was a denial personality inventory. As patients were referred for convulsive therapy, we interviewed a relative in an unstructured, exploratory interview. The questions were designed to determine the degree to which the patient approximated the explicit verbal personality type described by Weinstein and Kahn (3). On fifteen items, patients were scored on a three point scale of 0, 1 and 2. The scores were ranked and divided in half - those in the upper half were termed "high denial score" and those in the lower half, as "low denial score" (5).

We observed a significant relationship between the denial score and short term clinical ratings (Table 3). In addition, there was a significant relationship between the denial score and the number of clinical language changes during treatment (Table 4).

TABLE 3

RELATION OF DENIAL PERSONALITY TO CLINICAL RESPONSE TO ELECTROSHOCK

Personality Score	Much Improved	Moderately Improved	Unimproved	Total
11 to 25	14	9	1	24
0 to 10	7	9	7	23
Total	21	18	8	47

TABLE 4

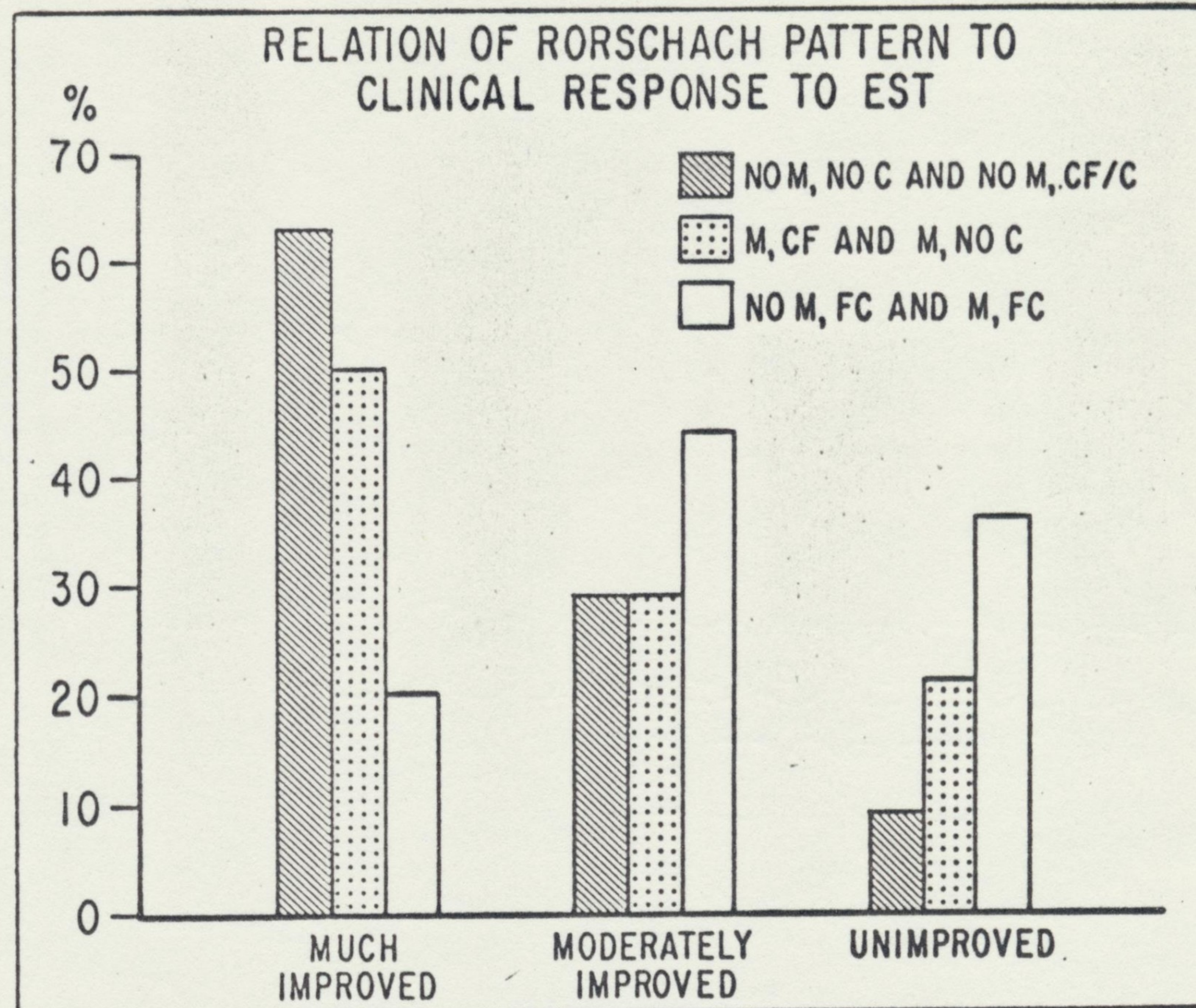
RELATION OF DENIAL PERSONALITY SCORES TO CLINICAL LANGUAGE CHANGES DURING TREATMENT

Personality Scores	Number Language Changes	
	0 - 2	3 or more
11-25 (20)	8	12
0-10 (20)	17	3
Total	25	15

c. Rorschach Determinants. Another task essayed was the Rorschach. We did not look upon this test in the usual interpretive manner, but scored the number and patterns of Rorschach determinants following the schemata of Klopfer and Kelley (6).

It was observed that ratings of much improved and recovered were associated with the following Rorschach criteria; absent human movement (M), absent form color (FC), few responses, high form percentage (F), presence of color (C) and color form (CF) or absence of all color, and low shading response. One schedule is reproduced in Figure 1 (7).

FIGURE 1



d. California F Scale. Still another attitudinal task is the California F Scale. This simple task consists of a series of 10 uncritical, global statements to which the subject is asked to express the extent of his agreement or disagreement. High scores reflect high agreement, and low scores, high disagreement (8).

There was a significant correlation between high F scores and favorable clinical ratings (Table 5). In addition, we also carried out social factors studies (9, 10) and reported that favorable outcome was associated with few years of education, foreign birth, and older age.

TABLE 5

RELATION OF SOCIAL FACTORS TO DISCHARGE RATINGS IN CONVULSIVE THERAPY

	N	Mean F Score	Mean Age	Mean Years Education	% Foreign Born
Recovered	8	53.1	51.6	9.4	50
Much Improved	26	41.8	43.8	10.6	35
Improved and Unimproved	23	39.7	32.3	12.3	17

Conclusion

In summary, we have observed that a variety of pre-treatment measurable aspects of behavior, usually described as personality variables, are associated with the development of the euphoric-hypomanic adaptive pattern in convulsive therapy and are rated as much improved or recovered in our setting. These variables have been defined in language patterns, denial scores on family interviews, perceptual style reflected in the Rorschach, California F Scale measure of attitude, and the social variables of age, educational level, and birthplace.

These personality and social variables provide the perceptual and attitudinal bases for the adaptive changes which occur under the conditions of altered brain function induced by repeated convulsions. Absence of these personality traits, in the presence of equivalent degrees of brain function leads to other adaptive patterns, usually rated as "improved" or "unimproved," and not to the euphoric-hypomanic mode.

The same theoretical model of the neurophysiologic - adaptive interactional hypothesis is applicable to drug therapy (2, 11). We would suggest that different agents are psychopharmacologically useful to the extent that brain function is altered systematically. These can be measured by the electroencephalogram, although not exclusively. Under the conditions of persistent altered brain function, changes in adaptation will occur, dependent on pre-treatment personality variables. These can be specified, and studies now in progress at Hillside Hospital are assessing this model for various psychotropic agents.

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DR. LASKY:

Thank you Dr. Fink. Do members of the panel have any questions or comments?

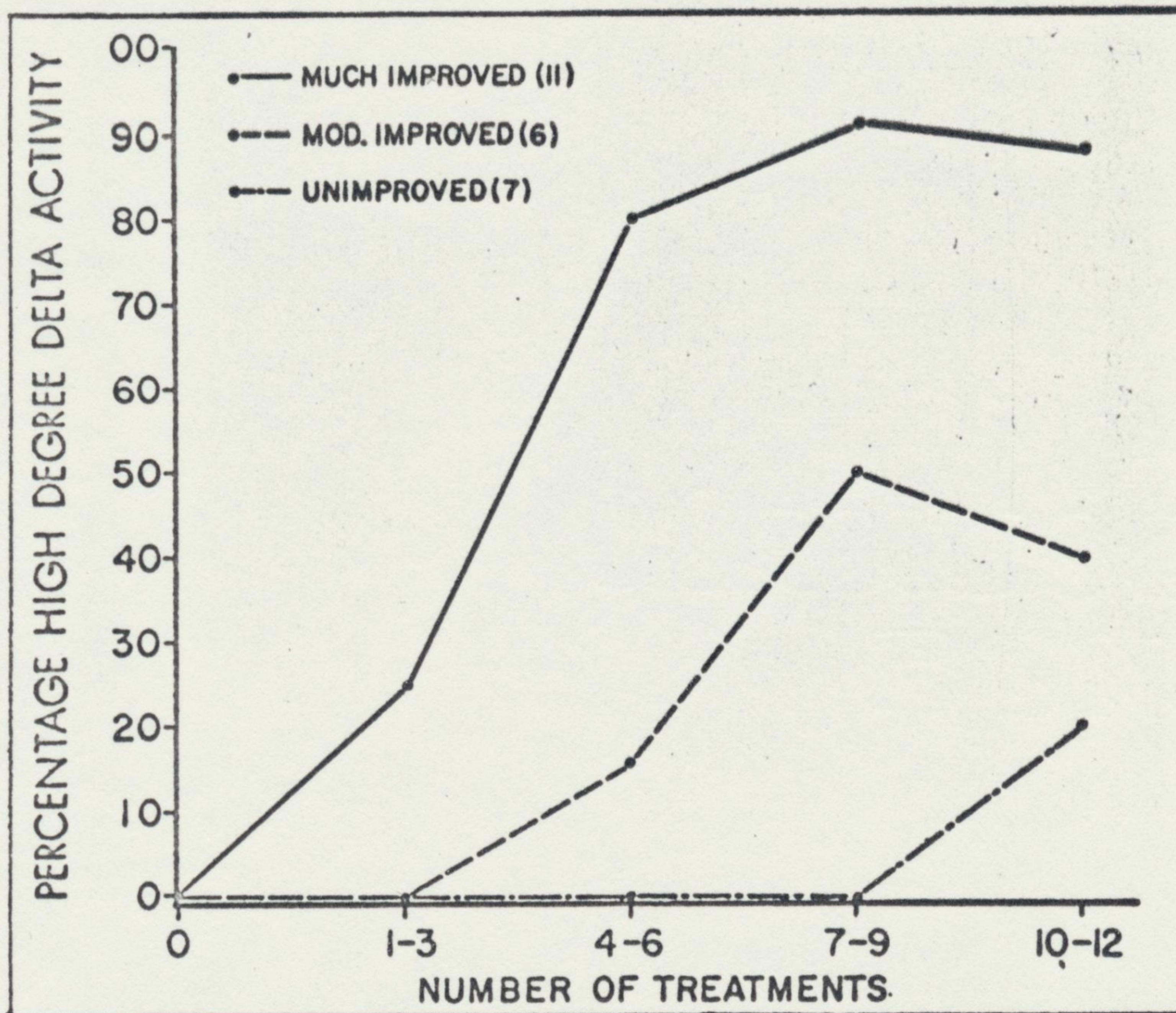
DR. KLERMAN:

Max, you presented with a fair amount of specificity, the personality and social factors which characterize the patient. I was disappointed in that the other half of your neuro-adaptive scheme was left unspecified. Namely, is there any specificity in the alteration of brain function that is as predictive as these specific social and personality factors?

DR. FINK:

I think the answer to that is that we do have considerable specificity for the various treatments that we use. If I might have Figure 2. This Figure will show that we did use electroencephalographic measures. We were rating the EEG changes according to criteria which we called high degree-slow wave activity. This index could be specified and quantified. After determining which records were "high degree" slow wave activity, we were able to go back and look at the patients who had shown the much improved category, the moderately improved and the unimproved. It is apparent that of the patients who were in the much improved group, about 90% of the records of that group had shown high degrees of EEG change during the third and fourth weeks of treatment. It is also clear that the patients who were "unimproved" did not show the high degrees of EEG change. We interpret these data to indicate that unless a patient has a high degree of EEG change he will not show behavioral change. It is necessary to have changes in brain function and it is under the conditions of the brain change that adaptive change will occur. The type of adaptive change depends on these personality variables. In drug therapy we have other EEG patterns which can also be specified.

FIGURE 2



DR. KLERMAN:

Is one difference between this kind of physiologic measure and the other measures in that they occupy different type predictive factor? Would you say here that unless the patient has this characteristic, EEG changes, he will not subsequently develop behavior and adaptive changes but can you predict before the treatment in any physiologic way whether or not a given patient will manifest these characteristic delta wave changes? In other words there is a difference between a predictive variable that you described as existing or characteristic with the patient prior to his exposure to the treatment and a predictive variable that says he must experience a certain kind of change under the influence of the somatic therapy.

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DR. FINK:

I think what you are asking is whether we can predict the physiologic response of the patient. I think we can, although this is much more difficult than predicting the behavioral adaptation. We still do not know what the determinants are or how to measure them prior to treatment, to predict whether a person will or will not show a drug response or will or will not show a physiologic response. The question is not one of a sequence, where altered brain function comes first and then the subjects involuntarily adapt to it. These processes are concurrent. At the time that brain function is changing under the influence of repeated convulsions or under the influence of repeated doses of drugs, the perceptual, the attitudinal, the conceptual and all the other aspects of patient behavior are undergoing change so that his whole view of life and his response to his environment is changed. The kind of change he shows depends on his pretreatment propensities, as we tried to show on electroshock.

DR. LASKY:

Dr. Fink, we'll ask another question or two. They are short ones. I think Dr. Gottschalk and I have something rather similar in mind. Now, the one I had was--Could you comment on your criterion. You used a three level over-all clinical rating of recovery, much improved and improved. Now the question that comes to my mind is why use such a crude criterion when you are using rather quantitative measures as predictors and ties in with that, of course, what does this criterion mean that a man is "improved"?

DR. FINK:

Dr. Gottschalk, do you want to ask something?

DR. GOTTSCHALK:

Well, I had a somewhat similar question, but I have focused on something a bit more specific than that--As whether Dr. Fink had any idea why those people with lower educational levels tended to have more improvement, was this possibly because of the goals being less as compared say to persons with higher educational levels, then of course this has some relationship to the question about the criterion for improvement.

DR. FINK:

I think that both these questions are crucial ones. I tried to indicate that our slides reflect early aspects of our studies. At the time that we did these first studies, we did not know what we were using as the eventual criterion of behavioral change. We used psychiatric ratings much as everybody else. This criterion was fairly effective. In the course of these studies, we learned that there were different behavioral modes, and these seem a more meaningful criterion. We are now in the process of assessing patients going through our electroshock program, trying to predict these various modes. Unfortunately, the number of patients referred for electroshock in 1960-61 has dropped off precipitously, so that we do not have a large enough sample. But, the statement of the slides on recovered and much improved reflects, as we look back in our data, those patients who showed the euphoric-hypomanic adaptation. That adaptation can be characterized by a feeling of well-being; an attitude on the ward of being fine; dressing up, and participating; and on inquiry stating they are no longer sick or depressed and that there is nothing wrong with me. Such behavioral changes are the ones that psychiatrists rate as much improved. In our hospital, which is psychodynamically oriented, there are a number of psychiatrists who have seen this adaptation and have said that this is not improvement, but explicit denial is a psychotic adaptation. There is, therefore, a problem of evaluating what we mean by much improved or unimproved. The question about educational level is also related. The evaluation of "much improved" is dependent on the psychiatrist's or the evaluator's attitude. This is one of the reasons why the use of much improved characterizations across hospitals is almost impossible. We tried to show this yesterday in Dr. Pollack's report of our tri-hospital study where discharge ratings did not have the same meaning in the various hospitals. The educational level is important because there is something about being well educated in the American culture which does not lend itself to the use of the gross denial

response. The more primitive cultures as we see them, and in our institution this is reflected in the people in the older age group who were born in Europe and who may have sustained their early life processes in Europe, that such people can use the adaptation or do use the adaptation of explicit verbal denial. Our more intelligent, younger, American born girls and boys just don't use gross denial.

The use of improved categorization is very poor and I must apologize for the use on the slides, but I had to use it because that is the way we started our studies. The next series of slides, hopefully a year or two hence, will not have that, but will reflect an adaptive mode typology. Then we hope that these predictors which we think we have teased out using improving categories will be effective in demonstrating those differences.

DR. LASKY:

Thank you very much, Dr. Fink. Our next speaker is Dr. Louis A. Gottschalk, who is Associate Professor and Research Coordinator at the Department of Psychiatry, Cincinnati General Hospital. The title of his paper is "Measuring Individual Response to Psychoactive Drugs by an Introspective Method and a Verbal Behavior (or Free-Associative) Method." Dr. Gottschalk.

MEASURING INDIVIDUAL RESPONSES TO PSYCHOACTIVE DRUGS BY AN INTROSPECTIVE METHOD AND A VERBAL BEHAVIOR (OR FREE-ASSOCIATIVE) METHOD ^{1/}

Louis A. Gottschalk, M.D.

Introduction

Measuring the individual and idiosyncratic responses to psychoactive drugs is a research area of increasing interest to investigators. The serious and systematic study of such phenomena is made difficult and compounded by the fact that the collective effect of the psychoactive drug has to be accurately measured at the same time that the unique and individual effect is being validly observed and, whenever possible, accounted for plausibly at some level of organization.

Approaches to this problem of detecting, measuring, and accounting for the individual response to psychoactive drugs have been many and ingenious. Some of the principal methods have been: 1) The administration of a drug to groups of patients with different major psychiatric nosological syndromes and looking for different patterns of behavioral and subjective reactions according to the diagnostic category, e.g., schizophrenia, psychoneurosis, etc., (Beringer, 1927; Hoch, Cattell, and Pennes, 1952 and 1953; Bensheim, 1929; Weinstein, 1953 and 1954; Kornetsky, 1960). 2) The determination of the relationship of varying individual responses to a drug associated with different personality profiles or behavioral patterns--such as, extraversion, depression, hysteria, etc.--as measured by various psychologic inventories or tests or clinical psychiatric evaluations (Kornetsky and Humphries, 1957; Lasagna, et al., 1955; Lavery, 1958). 3) The assessment of the individual reactions to a drug associated with a psychodynamic conflict, such as, a fear of dependence (Gottschalk, et al., 1956; Sarwer-Foner, 1957). 4) The investigation of different reactions to placebos (Beecher, et al., 1955 and 1956; Wolf, et al., 1950 and 1955; Kurland, 1960), which provide an indication of the sometime powerful placebo effect and hence the individual placebo component of the reaction to a drug.

^{1/} From the Department of Psychiatry, University of Cincinnati, College of Medicine. These investigations have been supported in part by a research grant (MY-1055) from the National Institute of Mental Health, Department of Health, Education and Welfare.

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**Aided, in part, by grants M-927 and MY-2715 of the National
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**Presented at the 6th annual V.A. Research Conference,
Cincinnati, March, 1961.**

IV: 4/13/61

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To determine the population prone to show this adaptive pattern (and therefore be rated as much improved and recovered) we eschewed the usual diagnostic terms or symptom check list, and sought more measurable aspects of behavior. During these studies we had developed a concept of the convulsive-therapy process which we termed the neurophysiologic-adaptive view (2). In this view, repeated convulsions are seen as a device to alter brain function. Under the conditions of such altered brain function behavioral adaptations emerge based on individual personality, socio-cultural and attitudinal factors. Thus, we sought measures of pre-treatment personality and attitude as predictive indices.

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RESULTS:

A. Language measures

Our first assessment was of language patterns. Earlier studies by Weinstein and Kahn (3) had demonstrated that patients with brain dysfunction had characteristic language changes of denial, disorientation and confabulation after intravenous amobarbital. In one electroshock study we observed that these same language changes occurred with increasing numbers of treatments. We also noted that those patients showing these language changes were the ones evaluated as recovered, while those not exhibiting the changes were generally rated as unimproved. A linguistic content analysis showed the language patterns rated in the study to be explicit denial, minimization, displacement, evasion, cliches, cryptic comments, use of third person, change of tense, withdrawal, qualification, and responding with a question (4).

It seemed probable that the subjects who showed these language patterns after electroshock would be the ones who have a propensity to using such patterns before treatment -

if we could elicit the language changes by some provocative test. We, therefore, tested each patient before electroshock by asking questions in a short structured interview, administered amobarbital until there was slurred speech and nystagmus, and then repeated the questions (3). We scored the answers for the number of language changes after amobarbital (4).

We noted a relation between the number of pre-treatment language pattern changes following amobarbital to the number of language changes manifested clinically during the fourth week of treatment (Table I). Furthermore, there was also a relationship between the number of pre-treatment language changes and short term clinical ratings of much improved and recovered (Table II).

Tables I, II

B. Family Interviews

Our second assessment was a denial personality inventory. As patients were referred for convulsive therapy, we interviewed a relative in an unstructured, exploratory interview. The questions were designed to determine the degree to which the patient approximated the explicit verbal personality type described by Weinstein and Kahn (3). On fifteen items, patients were scored on a three point scale of 0, 1 and 2. The scores were ranked and

divided in half - those in the upper half were termed "high denial score" and those in the lower half, as "low denial score" (5).

We observed a significant relationship between the denial score and short term clinical ratings (Table III). In addition, there was a significant relationship between the denial score and the number of clinical language changes during treatment (Table IV).

Tables III, IV

C. Rorschach Determinants

Another task essayed was the Rorschach. We did not look upon this test in the usual interpretive manner, but scored the number and patterns of Rorschach determinants following the schemata of Klopfer and Kelley (6).

It was observed that ratings of much improved and recovered were associated with the following Rorschach criteria; absent Human movement (M), absent form color (FC), few responses, high form percentage (F+), presence of color (C) and color form (CF) or absence of all color, and low shading response. One schedule is reproduced in Table V (7).

Table V

D. California F Scale

Still another attitudinal task is the California F Scale. This simple task consists of a series of 10 uncritical, global statements to which the subject is asked to express the extent of his agreement or disagreement. High scores reflect high agreement, and low scores, high disagreement (8).

There was a significant correlation between high F scores and favorable clinical ratings (Table VI). In addition, we also carried out social factors studies (9,10) and reported that favorable outcome was associated with few years of education, foreign birth, and older age.

Table VI

CONCLUSION:

In summary, we have observed that a variety of pre-treatment measurable aspects of behavior, usually described as personality variables, are associated with the development of the euphoric-hypomanic adaptive pattern in convulsive therapy and are rated as much improved or recovered in our setting. These variables have been defined in language patterns, denial scores on family interviews, perceptual style reflected in the Rorschach, California F Scale measure of attitude, and the social variables of age, educational level, and birthplace.

These personality and social variables provide the perceptual and attitudinal bases for the adaptive changes which occur under the conditions of altered brain function induced by repeated convulsions. Absence of these personality traits, in the presence of equivalent degrees of brain function leads to other adaptive patterns, usually rated as "improved" or "unimproved", and not to the euphoric-hypomanic mode.

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TABLE I

Relation Between Pretreatment Language Response to
Amobarbital Sodium and Clinical Changes and
Withdrawal During Treatment

	No.	Three or more clinical lan- guage patterns*	Withdrawal reac- tions to amobar- bital sodium†
Pretreatment response to amo- barbital sodium	30	18 60 per cent	21 70 per cent
No pretreatment response to amo- barbital sodium	35	11 31	12 34

* $\chi^2 = 4.26; P < .05$

† $\chi^2 = 6.88; P < .01$

TABLE II

Relation of Pretreatment Language Changes With
Amobarbital Sodium to Eventual Clinical Response

<u>Change</u>	<u>No.</u>	<u>Change with amobarbital sodium*</u>	
Much Improved	28	19	68 per cent
Moderately Improved	22	8	36
Unimproved	15	3	20

* $\chi^2 = 10.30$; $P < .01$

TABLE III

Relation of Denial Personality to Clinical Response
to Electroshock

	<u>Much</u> <u>Improved</u>	<u>Moderately</u> <u>Improved</u>	<u>Unimproved</u>	<u>Total</u>
<u>Personality Score</u>				
11 to 25	14	9	1	24
0 to 10	7	9	7	23
Total	21	18	8	47

TABLE IV

Relation of Denial Personality Scores to Clinical
Language Changes During Treatment

<u>Personality Scores</u>	<u>Number Language Changes</u>	
	0 - 2	3 or more
11-25 (20)	8	12
0-10 (20)	17	3
Total	25	15

TABLE V

Relation of Rorschach Factors to Clinical
Response in Convulsive Therapy

	N	Much Improved	Moderately Improved and Unimproved
Human Movement (M)	39	11 (28%)	28 (72%)
No Human Movement	48	28 (58%)	20 (42%)
		$\chi^2 = 6.76^* p < .01$	
Form Color (FC)	34	7 (21%)	27 (79%)
No Form Color	53	32 (60%)	21 (40%)
		$\chi^2 = 11.57^* p < .001$	
Both M and FC	24	4 (17%)	20 (83%)
Either M or FC	25	10 (40%)	15 (60%)
Neither M nor FC	38	25 (66%)	13 (34%)
		$\chi^2 = 14.83 p < .001$	

*With Yates' correction for discontinuity.

TABLE VI

Relation of Social Factors to Discharge
Ratings in Convulsive Therapy

	<u>N</u>	<u>Mean F Score</u>	<u>Mean Age</u>	<u>Mean Years Education</u>	<u>% Foreign Born</u>
Recovered	8	53.1	51.6	9.4	50
Much Improved	26	41.8	43.8	10.6	35
Improved and Unimproved	23	39.7	32.3	12.3	17