A Biometric Approach to Diagnosis and Evaluation of Therapeutic Intervention in Schizophrenia

Joseph Zubin, Ph.D.

In honoring me with the Stanley R. Dean Award, the American College of Psychiatrists and Fund for the Behavioral Sciences are recognizing not only my own contribution to the study of schizophrenia, but that of our entire Biometrics Research Unit established in January 1956, exactly 17 years ago, by the late Dr. Paul H. Hoch, then Commissioner of Mental Hygiene of the State of New York. The mandate received for this Unit was to develop an objective assessment of the behavior of the mentally ill with the purpose of improving diagnosis, prognosis, and evaluation of treatment and outcome*. Some of the contributions of this unit will be the substance of this chapter.

*The unit viewed its mandate through a wide-angled lens which included problems requiring the efforts of the following nine sections, each with its own staff and head, which were gradually added to the unit: (1) Anthropology, Dr. Muriel Hammer; (2) Behavior Analysis and Modification, Dr. Kurt Salzinger; (3) Biostatistics, Dr. Joseph L. Fleiss; (4) Diagnosis and Psychopathology, Dr. Barry J. Gurland; (5) Evaluation, Dr. Robert L. Spitzer; (6) Family Research, Dr. Denise Kandel; (7) Gerontology, Dr. Ruth Bennett; (8) Psychophysiology, Dr. Samuel Sutton, and (9) Sociology, Dr. David Wilder.
Many readers probably wonder what biometrics has to do with psychiatry and how such strange bedfellows as measurement and clinical research ever got together. Yet we have had a biometric tradition in psychiatry at least since the days of Esquirol, one of the first to count the number of patients according to the precipitating cause of their illness, finding some 25% were “love casualties.” Jaspers (1) noted the importance of biometrics, as did Kraepelin (2) and Freud.

Freud's interest in the biometric approach is exemplified in his correspondence with Fliess (May 25, 1895). He writes: “I am plagued with two ambitions: to see how the theory of mental functioning takes shape if quantitative considerations, a sort of economics of nerve-force, are introduced into it...” This ambition culminated in his Project for a Scientific Psychology (3). Originally he believed that measurable physical-chemical forces in the neurons underlay human behavior and they were sufficient to explain behavior without recourse to extraneous unquantifiable forces. While he gave up some of this belief later because of his inability to explain hysteria on a physical-chemical basis alone, his early efforts had a strong biometric undertone. This trend in attempts at measuring the energy of the neuron also characterized the early work of the New York State Psychiatric Institute when it was established before the turn of the century. Van Gieson and Sidis in 1898 developed a rather complex neurotic energy model to explain normal and abnormal behavior (4).

In the ’20s the first application of biometric methods to psychopathology was the testing of Henry Cotton’s focal infection theory (5), which was demolished through the work of Kopeloff and Cheney (6) in the first clinical trial of a therapeutic method in psychiatry.

There followed a period of relative stagnation in biometric activity, until World War II opened the opportunities for biometric investigations through the support of federal funds. Now, a number of centers exist in which biometric activities are pursued, notably at NIMH in the Biometric Branch under the guidance of Dr. Morton Kramer.

There are certain prerequisites for the biometric approach to a given problem. We must have at least an operational definition of the area under investigation and reliable and valid objective tools for carrying out the investigation. It is not easy to further define the biometric approach to psychopathology. Essentially it derives from the dicta of Lord Kelvin, who postulated that unless you can measure something, you do not understand it, and from Thorndike, who postulated that whatever exists, exists in some amount, and therefore ought to be measurable.

In the early ’30s I entered the field of psychopathology, fresh with a Ph.D. in psychology, and bringing the tools of experimental methods and design, statistical techniques, and mathematical reasoning with me to my first job at the Psychiatric Institute, ready to apply them to the mentally ill. But I soon faced the hard reality that the philosophy then current was psychoanalysis, which had no room for measurement, and even considered it a threat to treatment.

Despite this prevalent zeitgeist, I managed to take a few tentative steps into the field. When I was still a graduate student I dared, with the help of a few colleagues, to attempt a test of the tenability of one of Freud’s fundamental assumptions—the Oedipus Situation. We tried to develop a test which would examine the relative preference of children for parents of the same or opposite sex. Among the test items were such as, “Suppose you were out in a canoe with both of them and could only save one, whom would you save?” The results indicated that Freud was right; namely, up to about age 6 there was a definite preference for the parent of the opposite sex and at age 6, apparently, the latency period had set in and even the girls preferred mother. We waited for a long time after sending all
this material, together with statistical tables, to Freud before receiving his answer: “ganz amerikanisch, but I do not quite see what you can prove with your statistics.” Taken aback by this refusal to accept verification, I inquired of some of my psychoanalytic friends as to what might have been the difficulty. I was told: “Suppose you came to the Pope with proof that God exists. What do you suppose he’d say?”

I then turned my attention to the most frequently used clinical tools of the ’30s and ’40s: self-report inventories, projective techniques, handwriting analysis, and sorting tests. I found each of these wanting, not because they were intrinsically invalid, but because of two basic difficulties: (a) responses to these techniques depended on the unique history of the individual and its reflection of the particular ecological niche in which he had developed, and (b) there was an absence of any criteria other than the clinical interview for validating the findings of these techniques. Even the value of the Rorschach technique vanished when it was regarded as a test (7).

The clinical interview, despite its primary usefulness in determining the presence or absence of psychopathology, was itself extremely unreliable, as many studies had shown. If it were to be used as the criterion for evaluating more objective aspects of behavior, it would have to become more objective and reliable. Thus, our Biometric Research Unit began to develop systematic structured interviews in which each question was accompanied by several possible response items. The presence or absence of each item could be recorded by the interviewer.

The mental status schedule, which had been the psychiatrist’s mainstay, was converted into this kind of systematic structured interview in our laboratory, yielding high reliability in scoring of items, as well as considerable validity. We worked with three types of interviews: (a) a non-probing approach—Structured Clinical Interview (SCI) by Burdock and Hardesty (8); (b) a medium-probing—Mental Status Schedule (MSS) by Spitzer, Burdock, and Hardesty (9), and Psychiatric Status Schedule (PSS) by Spitzer, Endicott, Fleiss, and Cohen (10); and (c) a deep-probing—Present State Examination (PSE) by Wing, Birley, Cooper, Graham, and Isaacs (11).

Another reason we tried to objectify the clinical interview and render it more reliable and valid arose from our comparative international studies of diagnoses of mental disorder in the United States and the United Kingdom, undertaken by the Section on Diagnosis and Psychopathology of our unit. Faced with the report by Dr. Kramer (12) that the rate for manic-depressive psychosis was 10 times higher in the U.K. than in the U.S., and that the rate of schizophrenia, on the other hand, was much higher in the U.S. than in the U.K., we launched a study to determine the causes of this differential.

Using a combined schedule of non-probing, medium-probing, and deep-probing items, our Project on Diagnosis of Mental Disorders in the United Kingdom and the United States* was able to demonstrate that the much heralded differences in the incidence of hospitalized functional mental disorders (schizophrenia versus affective psychosis) in the United States and the United Kingdom were actually labeling differences (13, 14).

It appears that though British and American psychiatrists are equally sensitive to the presence of psychopathology in mental patients, American psychiatrists are inclined to use the label “schizophrenia” more and the label “affective disorders” less than the British.

One of the incidental, but most exciting, results of the development of systematic structured interviews and their application to large groups of mental patients is the possibility of laying down a new anatomy of psychopathology by dissecting out its underlying dimensions through statistical techniques such as factor analysis or typological analysis. Such an analysis yielding

* Headed by Dr. Barry Gurland in the United States and Dr. John Cooper, now succeeded by Dr. John Copeland, in the United Kingdom.
factor analyses. In our study, we succeeded in separating these factors in two. The key items in the flat affect factor are:

"Patient maintains a facial expression lacking signs of emotions,"

"Absence of normal variation in patient’s tone of voice,“ and

"Patient talks of his condition with no outward sign of emotions."

The key items in the retardation factor are:

"Patient pauses a long time before replying to questions,“

"Patient walks abnormally slowly,” and

"Patient speaks slowly."

To facilitate comparisons between diagnostic groups, all scores were standardized to a mean of 50 and a standard deviation of 10. These diagnoses were the final diagnoses arrived at by the project team of the U.S.-U.K. diagnostic study.

Figure 1 presents mean standard scores for all schizophrenics and all depressives. The difference between the two groups on retardation is small (t = 1.10 [not significant]). The schizophrenics scored significantly higher than the depressives on flat affect, however (t = 3.35, p < .01). It is thus the flat affect component of apathy and lethargy, and not the retardation component, which helps in distinguishing between schizophrenia and depression.

Figure 2 illustrates how the retardation component is important in separating depressives into neurotic and psychotic subtypes. The psychotic depressives score significantly higher than the neurotic depressives on retardation (t = 3.07, p < .01), but were not significantly different on flat affect (t = 0.97, [not significant]).

Both flat affect and psychomotor retardation are important for diagnostic discriminations. The means now exist to measure each without contamination by the other.
The Evaluation Section of our unit under the direction of Drs. Spitzer and Endicott has developed standardized techniques for evaluating psychopathology and role functioning of patients and nonpatients to facilitate (a) comparing patient and nonpatient populations with regard to current and past mental health status, prognosis, and diagnosis; (b) evaluating different treatment programs and approaches; and (c) studying other substantive issues of etiology, treatment, and course of mental disorders.

These techniques have been shown to discriminate among subgroups of schizophrenics and to differentiate schizophrenics from other diagnostic groups. Two computer programs for diagnosis have been developed, each taking the results of psychiatric examinations as input. The program acts like a clinician in asking a series of questions of the data, and then yields a psychiatric diagnosis. The computer-derived psychiatric diagnoses have been shown to have a high agreement with clinical diagnoses made from the same data.

I have, thus far, indicated how our Biometrics Research Unit came to be interested in the better description of schizophrenia. Let us now go further in developing the topic of the evaluation of therapeutic intervention.

Therapeutic intervention may be defined as planned treatment of a disorder with the view to eliminating, or mitigating, or arresting its progress. To intervene effectively, we must first know (a) the nature and identity of the disorder, (b) the point in time at which to intervene, (c) how to intervene, (d) the method to use most effectively, and (e) how to evaluate the efficacy of intervention.

We must confess at the very start that when we look at the five areas of knowledge which we require, we are, in fact, facing voids. We do not know the nature of the disorder labeled schizophrenia; we cannot diagnose it accurately; we do not know the ideal moment to intervene or how to intervene, what method to use or how to evaluate it. Although we are abysmally ignorant, we must make do with whatever pragmatic knowledge practitioners have collected in the course of time. But we must not accept them at face value. It is necessary to lay bare the knowledge we have inherited in order to examine its tenability.

As far as the nature of the disorder is concerned and how it is to be identified, we must attempt to provide a definition if
we are to communicate with others regarding the results of our investigations. As all of us are aware, no common agreement exists universally regarding mental disorders and especially regarding schizophrenia. How can this impasse be surmounted?

First, is it really necessary to provide an ironclad definition of schizophrenia? Is it necessary that a category be defined rigidly in a closed-ended way, like a mathematical concept? If this were necessary, such widely useful concepts as "species" would go by the board. Julian Huxley (15) has pointed out that: "... there is no single criterion of species. Morphological difference; failure to interbreed; infertility of offspring; ecological, geographical, or genetical distinctness—all those must be taken into account, but none of them singly is decisive. Failure to interbreed or to produce fertile offspring is the nearest approach to a positive criterion. It is, however, meaningless in apogamous forms, and as a negative criterion it is not applicable, many obviously distinct species, especially of plants, yielding fertile offspring, often with free Mendelian recombination on crossing. A combination of criteria is needed, together with some sort of flair."

If biologists cannot define species rigorously, we need not be shamefaced that we cannot rigorously define schizophrenia. The test of a good definition is not ironclad rigor, but usefulness.

Second, we must distinguish between the presence and absence of a disorder in general. We might regard a disorder as a progressive condition which, unless adequately dealt with, will result in premature death, severe loss of efficiency, or severe reduction of happiness (or increase in excessive pain), or some, or all of these. A disorder is to be distinguished from a defect, which is a stationary condition that will result in severe loss of efficiency or in a reduction of happiness or both, but will not necessarily shorten life.

It is simple enough to accept premature death as a criterion of a disorder, but it is not a very useful one since it can be used only retrospectively (though it may be possible in the future to utilize this criterion by means of suitable prognostic indicators). The criteria based on loss of efficiency and reduction of happiness are difficult to apply since these criteria have no readily available baseline.

One suggestion for circumventing these difficulties* is to utilize the value judgment that society places on the condition in question. Thus, if most possessors of a given condition would gladly be rid of it or are actively searching for ways of eliminating it, we could utilize this information as an index for the presence of a disorder. The inverse is particularly illuminating: a disorder is a condition which most of those not possessing it would neither seek nor be willing to accept.

Another index of the presence of a disorder** is whether society is sufficiently troubled by the condition to provide methods for eliminating it or containing it, or is actively searching for such methods.

Thus, a disorder is an undesirable state from which relief is sought. Whether this definition is to be locally applied in each subculture or whether a universal classification is to be developed remains an open question. If methods for eliminating or containing a condition are universally provided or sought, the recognition of this state as a disorder offers no problem. If only a small group of individuals or some highly isolated culture regards a given condition as a disorder, it would probably not be generally accepted as such. Between these extremes is a continuum of growing consensus as to whether a given condition is to be regarded as a disorder, and the higher the consensus across cultures, the greater the probability of its acceptance. Thus, the term disorder, like the term species, has no rigorous definition. "A combination of criteria is needed together with some sort of flair." (15)

* Suggested by Dr. Robert L. Spitzer of our unit.
** Suggested by Dr. Barry Gurland of our unit.
Concerning schizophrenia, it is clear that it satisfies four of our criteria for being regarded as a disorder: it interferes severely with efficient living; it severely reduces happiness; those who don’t have it don’t seek it, and those who do have it generally wish to be rid of it; and wherever it is recognized, some treatment for it is sought.

For operational purposes, glossaries have been developed which specify characteristic behaviors that must be present for a given condition of a patient to qualify as schizophrenia. There are several such glossaries available and it is hoped that we will eventually accept a universal glossary such as the one proposed by the World Health Organization (16) that will serve the purposes of better communication across different nations and cultures.

The aim of such a glossary should be to ensure so far as possible that those who use it will apply diagnostic terms uniformly. Thus, it is less important that the diagnostic terms be “correct” than that like conditions should be classified under the same rubric, and that it should be known where a given syndrome or disease is being listed.

Even the availability of glossaries, however, cannot ensure an operational definition of a diagnostic term. To attain this desideratum, we must specify more clearly the way in which the information regarding a given person should be collected and the way the data obtained are to be integrated. Systematic structured interviews with predesigned item choices for recording have given an added reliability to the information collected, and computer programs either based on decision-tree procedures or utilizing Bayesian (17) approaches can provide better uniform integration of the data for diagnostic purposes. But these diagnoses, despite their high reliability and reproducibility, are no better than the clinician who developed the decision tree. Only continued follow-up studies relating the diagnosis to outcome of specific treatment, to duration of illness, to eventual

outcome, and so forth, can provide us with the validity criteria for the diagnosis, even though we have the highest degree of reliability.

Why is it that, despite the available techniques, it is still very difficult to diagnose schizophrenia accurately? One reason for the difficulty is the confusion between the disorder present in the patient and the illness which he exhibits. Adolf Meyer hinted at this necessary differentiation, but his suggestion was rarely implemented. If we define a disorder as the focal process and the corresponding illness as the combined effect of the focal process and the response of the patient to it, including the patient’s response to society’s attitudes, it becomes clear why the picture presented by schizophrenia is so heterogeneous and the variety of treatments so diverse. Until we can separate the focal disorder from its effect on the premorbid personality, i.e., the total picture presented by the illness, we shall be caught in an undecipherable puzzle.

Because of the great difficulty in defining schizophrenia, several prominent clinicians have begun to doubt whether schizophrenia really exists, or, if it does exist, whether, in fact, it is merely a life-style rather than a disorder. Rather than get into that thicket, however, I suggest that we recognize that all natural phenomena are approached from two aspects: facts and fictions. Facts deal with the ostensible nature of objects and events—things you can point your finger at. Fictions are categories we use to hold facts together. Of facts, we ask if they are true. Of fictions, we ask only if they are useful. They remain useful only insofar as they serve some good purpose, such as the selection of therapy, prediction of outcome, etc. For this reason, the question of whether schizophrenia is a myth must be altered to whether schizophrenia is a useful concept.

And what evidence do we have that the concept of schizophrenia is useful?

It has been claimed for some time that schizophrenia does
not observe cultural boundaries and is evenly distributed in all cultures—in other words, that schizophrenia is not merely the product of Western culture, but that it exists universally in all cultures and is an indigenous human condition. The recent WHO International Pilot Study of Schizophrenia (18) has provided direct evidence for this claim in investigating admissions to mental hospitals in nine Field Research Centers in the following countries: Colombia, Czechoslovakia, Denmark, India, Nigeria, Taiwan, the U.S.S.R., the U.K., and the U.S.A. A sufficiently wide-spectrum of 1202 patients warranted making cross-cultural inferences regarding the presence of schizophrenia.

A systematic structured interview of the type described earlier for the U.S.-U.K. study was administered, using items that differentiated significantly between those patients diagnosed as schizophrenic and those diagnosed in other categories. After some winnowing and sifting, 69 items had been selected and subjected to a discriminant function analysis to pick out the items that had the highest weight in separating the two contrasted groups. Twelve items were selected with the highest weights.

The items found to be indicative of schizophrenia were of three types, as shown in Tables A - D.

Table A gives the items which counterindicated schizophrenia. It will be noted that all of these items deal with disorders of mood and sleeping disturbance most characteristic of affective disorders and in this way ruled out schizophrenia.

Table B shows the items dealing with delusions.

Table C shows the items dealing with disturbance in communications and Table D shows the items dealing with poor insight and restricted affect.

When these 12 items were utilized as a 12-point scale and applied to each of the 1202 patients in the WHO project, it was possible to determine how many of the patients diagnosed as schizophrenic scored high or low on this new diagnostic scale.

### Table A

<table>
<thead>
<tr>
<th>Sign or symptom</th>
<th>PSE Observation or question</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waking early</td>
<td>Have you been waking earlier in the morning and remaining awake? (Rate positive if 1 to 3 hours earlier than usual.)</td>
<td>.83</td>
</tr>
<tr>
<td>Depressed facies</td>
<td>Facial expression sad, depressed.</td>
<td>.73</td>
</tr>
<tr>
<td>Elation</td>
<td>Elated, joyful mood.</td>
<td>.67</td>
</tr>
</tbody>
</table>


### Table B

<table>
<thead>
<tr>
<th>Sign or symptom</th>
<th>PSE Observation or question</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Widespread delusions</td>
<td>How widespread are patient's delusions?</td>
<td>.74</td>
</tr>
<tr>
<td></td>
<td>How many areas in patient's life are interpreted delusionally?</td>
<td></td>
</tr>
<tr>
<td>Bizarre delusions</td>
<td>Are the delusions comprehensible?</td>
<td>.69</td>
</tr>
<tr>
<td>Nihilistic delusions</td>
<td>Do you feel that your body is decaying, rotting?</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Do you feel that some part of your body is missing, for example, head, brain, or arm?</td>
<td>.70</td>
</tr>
<tr>
<td>Thoughts aloud</td>
<td>Do you feel that your thoughts are being broadcast, transmitted, so that everyone knows what you are thinking?</td>
<td>.95</td>
</tr>
</tbody>
</table>

Table C

<table>
<thead>
<tr>
<th>Sign or symptom</th>
<th>PSE Observation or question</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incoherent speech</td>
<td>Free and spontaneous flow of incoherent speech</td>
<td>.74</td>
</tr>
<tr>
<td>Poor rapport</td>
<td>Did the interviewer find it possible to establish good</td>
<td>.86</td>
</tr>
<tr>
<td></td>
<td>rapport with patient during interview?</td>
<td></td>
</tr>
<tr>
<td>Unreliable information</td>
<td>Was the information obtained in this interview</td>
<td>.73</td>
</tr>
<tr>
<td></td>
<td>credible or not?</td>
<td></td>
</tr>
</tbody>
</table>


Table D

<table>
<thead>
<tr>
<th>Sign or symptom</th>
<th>PSE Observation or question</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor insight</td>
<td>Overall rating of insight</td>
<td>.85</td>
</tr>
<tr>
<td>Restricted affect</td>
<td>Blank expressionless face.</td>
<td>.62</td>
</tr>
<tr>
<td></td>
<td>Very little or no emotion shown when delusion or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>normal material is discussed which would</td>
<td>.63</td>
</tr>
<tr>
<td></td>
<td>usually bring out emotion.</td>
<td></td>
</tr>
</tbody>
</table>


Table E

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of critical items</th>
<th>Percent attaining critical score</th>
<th>Percent failing to attain critical score</th>
<th>Percent attaining critical score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenic</td>
<td>4 or more</td>
<td>91</td>
<td>9</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>5 or more</td>
<td>80</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>6 or more</td>
<td>65</td>
<td>35</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>7 or more</td>
<td>41</td>
<td>59</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>8 or more</td>
<td>21</td>
<td>79</td>
<td>0</td>
</tr>
</tbody>
</table>


Table E shows the proportion of schizophrenics and of non-schizophrenics who could be classified correctly or incorrectly (false positives and false negatives) depending on the breaking point chosen of the 12-point scale.

Thus, if the breaking point is taken as 4, 91% of the schizophrenics are classified correctly and 9% are false negatives, but 33% of the non-schizophrenics would also be classified as schizophrenic, which is too high a proportion of false positives to be acceptable. However, if we take a score of 8 as our breaking point, 21% of the schizophrenics are correctly classified and not a single non-schizophrenic is misclassified—no false positives. This is accomplished at some sacrifice since 79% of schizophrenics fail to attain a sufficiently high score to belong, but the sacrifice may be worthwhile since, though we fail to include all schizophrenics, we succeed in eliminating the non-schizophrenic, thus producing a "core group."
Even though not all individuals labeled schizophrenic belong to the core group, no non-schizophrenic belongs to it, and, therefore, if one desires to select a group of schizophrenics about whom there would be a consensus, these 12 items can serve as a basis for selection.

If one is willing to run the risk of including a small proportion of false positives, he could select a group having only 6 or more critical items in common, and this would include about two-thirds of the total schizophrenic group and only 5% of the non-schizophrenics.*

Thus, it can be concluded that it is possible to identify a core group of schizophrenic patients which has a distinctive pattern of symptoms and that there are patients belonging to this group in every Center in the study.

Finally, the genetic evidence for the existence of a strain of schizophrenia is unmistakable. While the newly proposed hypothesis by Rosenthal, Wender, and Kety (19) for the inheritance of a schizophrenic spectrum rather than of a specific schizophrenic disorder is somewhat baffling, it nevertheless speaks for the usefulness of the concept of schizophrenia, if not for the existence of the condition itself. As Kety has pointed out, if it is a myth, it is an inherited myth!

Thus far we have dealt with the classification of hospitalized mental patients. How well do our diagnostic schemes hold up when we examine a sample of the general population? In other words, how well can we discriminate the well from the ill among those who do not come for help?

If we are to be fair to ourselves and to our colleagues, as well as to the public who put their trust in us, we must admit that we are not as successful in determining whether a given person who has not come for help belongs in a diagnostic category as we are in those who have come for help. Apparently, then, un-

---

* This study contained a self-replication, but the table gives the average results for the original sample and the replicated sample.
ment may go awry. The learning theory model is, simply, that man learns to become sick according to the same behavioral laws which govern his normal development. The internal environment model stipulates that the roots of man’s illnesses are to be sought in his metabolism, body fluids, and body chemistry in general. The neurophysiological model concentrates on the functioning of man’s nervous system and its capacity to take in and process information.

The evidence produced by these various models for causation of mental disorders would require a great deal of space, but I will try to provide a brief summary here.

**Ecological Model**

The evidence for the ecological model is based on studies of the relation of socioeconomic status to schizophrenia which Faris and Dunham (21) began in the ‘30s, and which have raised the troubling question of what is cause and what is effect. Does low economic status breed schizophrenia or does schizophrenia gravitate to low economic status? An exciting research design has been proposed by the Dohrenwends (22) to answer this question. But for the time being, the only evidence available for a causal link between sociocultural factors and schizophrenia is the work of H. B. M. Murphy (23) in his examination of data on admission rates for schizophrenia in a variety of ethnic groups composed of both Catholic and non-Catholic subgroups. Across all of the ethnic groups he studied, the Catholic subgroups invariably had the higher admission rates for schizophrenia in males. He tries a variety of possible explanations, among which are the abstemious asexual model for Catholic youth provided by the priest and the nun. Another possibility is that the males in Catholic families do not receive adequate preparation for competing in the outside world. It is possible, however, that the Catholic subgroups may utilize hos-
pital facilities more than the non-Catholic, and this may explain the observed difference.*

A rather striking example of social causation, or social labeling, is afforded by Ackerknecht (24) in his reference to reports that among some South American Indians a very disfiguring spirochaetal infection of the skin, known as pinto, is so widespread that almost all men suffer from it. The few who escape infection are regarded as ill and are precluded from marriage. If we were to liken the stressful pressures of the Puritan ethic for getting jobs and making a living as an infectious agent in our culture, we might emerge with the probability that the small percentage of our population who are not infected by the Puritan ethic might be regarded in some quarters as sick and often be prevented from marrying. This could in fact be the basis for labeling some individuals as schizophrenic.

**Developmental Model**

Perhaps one of the most vocal proponents of the developmental model is last year's Dean Award winner, Dr. Theodore Lidz. Dr. Lidz's (25) elegant classification of families into the schismatic and the skewed marks an advance in the taxonomy of family types and a most plausible basis for the development of schizophrenia. One can only marvel at the careful painstaking methods he has developed. Without controls, however, it is difficult to fathom whether Dr. Lidz is not actually providing us with a taxonomy of so-called normal family life. Whether his analysis will prove of value to schizophrenics and their families is a hopeful but yet-to-be-realized ambition.

Lidz's concept of centering, in which the child frees himself from parental dominance in favor of peer group relationships, lends itself to examination experimentally. As a matter of fact,

* This is found not to be the case for admissions for depression, but whether it holds true for schizophrenia is not yet known.

one of our former students, Dr. Dolores Kreisman (26), under our guidance, studied the development of adolescent friendship patterns during the preschizophrenic period and contrasted this with development in normals. The outcome indicated that while by and large there was no great difference in the number of friends, intensity of friendship, etc., there was one remarkable difference. The measure of intimacy differentiated the two groups significantly, the normals having the higher scores.

One of the principles prominent in developmental theory is the principle of critical periods—that certain events are crucial for the occurrence of certain types of developments if they occur at a critical juncture. Coming too early, they are ineffective; too late, the particular developmental progress is irretrievably lost. Thus, separation of neonate from mother may not be as crucial at age 6 days as at age 6 months. Similarly, being orphaned at age 5 is more critical than at age 15.

One of the most striking proofs offered for the role of family interaction in the development of schizophrenia comes from Bateson, Jackson, and Hailey (27) in their double-bind hypothesis. Here, too, unfortunately, while it is a very persuasive hypothesis, it fails to differentiate normal from abnormal families. Recent investigations have found normal families to be characterized by similar double-bind patterns.

Some of the most negative results on the question of family interaction as a force in the production of schizophrenia in the offspring come from an unexpected quarter, Manfred Bleuler, who has long had an interest in the importance of the family of schizophrenics, an area of interest first promulgated by his fellow countryman, Adolf Meyer. Bleuler's recent book (28), reviewed by Sir Aubrey Lewis (29), focuses on the interplay between patients' lives and those of their nearest relatives in the follow-up of 208 probands.

He found that from 5% to 7% of the parents of the schizophrenic probands were themselves schizophrenic, with mothers
affected twice as frequently as fathers. Thus, the vast majority of schizophrenics are raised by presumably normal parents.

Only 25% of the probands showed schizoid features premorbidly, with 18% schizoid in school. Only 14% came from homes in which conditions were appalling. Premorbid occupational levels were similar to that of the parents (fathers) and no different from the distribution in the general population, confirming an earlier study in England by Goldberg and Morrison (30). Unhappy conditions in childhood (broken homes and the like) were not related to deteriorating course in schizophrenia.

Death of parents seemed to have a salutary effect on 7 patients with a pronounced ambivalence towards their parents. Only 9% of the siblings of the probands were found to be schizophrenic.

Eighty-four percent of the married children of the probands were married happily even though they had been raised by schizophrenic parents. Three of the schizophrenic parents had schizophrenic spouses to whom a total of 5 children were born. Despite the double hazard of noxious heredity and family upbringing, 3 of the 5 were mentally healthy.

Bleuler’s findings would indicate that the effect of deviant family upbringing seems to be not as noxious as the literature claims.*

**Learning Model**

Several hypotheses have been proposed for the etiology of schizophrenic behavior based on learning principles. Among these are (a) superstitious behavior, (b) effects of intermittent reinforcement, and (c) conditioned reinforcement. In addition, Salzinger (31) of our unit has provided the immediacy hypothesis as an underlying explanation of schizophrenic behavior.

---


---

1. **Superstitious behavior**

This type of behavior occurs in situations where responses are “conditioned by reinforcers that are actually occurring at random (32).” Since temporal contiguity between response and reinforcer is all that is needed to establish conditioning, the subject cannot tell the difference between a reinforcer that the experimenter delivers and a reinforcer that happens to be contiguous to his response by sheer chance. Thus, it is quite clear why animals as well as humans will learn to do things for which there is no systematic “real reinforcement contingency.” Is it not possible that in a society as complex as ours, with all of its recurring stimuli, such chance stimuli might inadvertently and unnoticeably acquire control over some people’s behavior? Is this the basis for ritualistic behavior? Compulsive behavior?

2. **Intermittent reinforcement**

That even aperiodic non-systematic and non-continuous or inconsistent reinforcements may nevertheless condition behavior is an important factor in the utilization of learning theory in explaining abnormal behavior and its maintenance. The intermittent reinforcement literature tells us that the inconsistent reinforcing behavior by the mother and/or father most likely serves very strongly indeed, for all its inconsistency, in producing persistent abnormal behavior in the child. The fact that the mother tries very hard not to give in to the child’s temper tantrum, but gives in some of the time, is of course the very paradigm which maintains the behavior she is trying to eliminate. The fact that conditioning is more rapid than extinction also makes the intermittent schedule a good candidate for the production of abnormal behavior.
3. **Conditioned reinforcement**

Events associated with primary reinforcers can themselves become reinforcers. The conditioned reinforcer may also help to explain such seemingly bizarre behavior as the collection of magazines or rags or other apparently worthless objects by patients. That such collecting behavior can be practically eliminated by procedures Ayllon (33) calls “satiation” may simply demonstrate a way of reducing the effectiveness of a conditioned reinforcer (rags or magazines) by presenting it frequently in the total absence of any other reinforcers (primary or conditioned).

A variety of learning theory models are described in a recent book by Salzinger (31), head of our Section on Behavior Analysis and Modification. Among these theories are those of Mednick and of Rodnick and Garmezy, all holders of the Dean Award in former years. I will not detail them at length, but will briefly describe Salzinger’s Immediacy Hypothesis as an explanation of schizophrenic behavior. You will note that unlike the other models which have tried to explain schizophrenia as due to some underlying disorder, learning theory models do not postulate an underlying disorder, but regard the specific behavior of the schizophrenic as “das Ding an sich”—the disorder itself—and try to indicate how it is maintained and why it continues to occur, regardless of how it may have arisen.

The primary source of schizophrenia, according to Salzinger’s approach, is some dysfunction in stimulus control—the schizophrenic’s response to stimuli in both the external and internal environment. Unlike normals who view the environment broadly, including both proximate and distant objects and events in time and space, the schizophrenic, according to Salzinger, is bound to respond to immediate stimuli in time and space, and this confinement to immediate stimuli in his responses, interacting with the laws of learning, is sufficient to explain schizophrenic behavior. Since immediately close stimuli are not always the most relevant, the schizophrenic, because of his attraction to immediate stimuli, will appear to respond irresponsibly. This may also explain why the schizophrenic will be more likely to expose himself to stimuli which normals consider aversive, particularly the conditioned aversive (social) ones, since these stimuli would be aversive to him only if he responded to them in terms of their remote conditioning history—something he fails to do. Primary aversive stimuli will, however, be avoided, as is the case with normals, only more so for the schizophrenic, since the primary attributes of the aversive stimuli cannot be adapted to by conditioning as readily as is the case with normals:

The hypothesis explains schizophrenics’ deficit in object constancy by calling attention to the fact that the retinal image is more immediate as a stimulus than the history of the object being viewed. Although the theory states nothing specifically about slower reaction time in schizophrenics than in normals, it follows that a person whose behavior is controlled by immediate stimuli might show a slower response to a given stimulus if other stimuli are present to capture his attention. In the case of no special reinforcement contingency, the immediate stimuli are irrelevant and produce the typical schizophrenic longer reaction time; when there is a reinforcement contingency, then the immediate stimuli reinforce the shorter reactions times... (p. 140). (31)

**Genetic Model**

The genetic model was in the doldrums for a while because some of its exaggerated claims based on twin studies were deflated during the ’60s, but it has received a surge of new interest as a result of the investigation of high risk populations begun by one of the former Dean Award winners, Mednick (34), and
and behavioral investigations today is how to purify the control group by eliminating unexpressed schizophrenic genotypes.

**Internal Environmental Model**

The internal environmental model has also been in the doldrums until recently because most of the earlier findings seemed to be non-specific to schizophrenia. Beginning with Kety's investigation of cerebral blood flow in schizophrenics in 1948, an important milestone in studies of the internal environment in schizophrenia, the investigations following this etiological model have spread rapidly and widely. Cerebral blood flow did not differentiate schizophrenics as a group and succeeding studies of peripheral metabolic correlates met the same fate. It was not until central synaptic mechanisms became the focus of attention that progress was seen. The advent of drugs which influenced the central nervous system allowed correlation between biochemical action and clinically observable subjective states. Although many leads turned into blind alleys during the last two decades, as Kety (35) points out in his recent Paul Hoch Award address, two hypotheses emanating from this early work are still very promising and have led Kety to assume a very optimistic stance regarding further progress. The findings I am reporting here are drawn from Kety's paper.

The first is the transmethylation hypothesis, based on which nicotinamide was suggested as a treatment for schizophrenia since it is a methyl acceptor and would be expected to drain away from the abnormal pathways methyl groups which permitted an accumulation of methylated hallucinogenic substances. Although this treatment turned out to be a failure, the transmethylation hypothesis received support from another quarter. When methionone, which favors transmethylation, was administered, it exacerbated psychotic behavior in a significant proportion of schizophrenics, but produced no effect in normals. Despite considerable controversy regarding possible alternative explanations, transmethylation is still a viable hypothesis.

---

The second hypothesis postulates that the disturbance in central catecholamine synapse may account for the crucial vulnerability of the schizophrenic. Evidence for this comes from the great similarity between the toxic psychosis induced by amphetamine and schizophrenia. Since amphetamine releases dopamine and norepinephrine at catecholamine-containing nerve endings, Snyder and his group (36) attempted to determine which of these two types of nerve endings were involved in amphetamine-produced psychotic and stereotyped behavior in man and animals. They concluded that dopamine rather than norepinephrine receptors were involved.

Further evidence for this hypothesis came from the finding that phenothiazines produced a blockade of dopamine receptors in the brain. Thus, if the psychosis produced by amphetamine is analogous with endogenous psychoses, and if both are in some way related to some malfunction in dopaminergic systems, then one can appreciate that the alteration in dopamine metabolism produced by phenothiazine can ameliorate schizophrenic behavior. It will be fascinating to see how the detailed mechanisms of action of these two different drugs, amphetamines and phenothiazines, will eventually explain this.

Furthermore, if the analogy between amphetamine psychosis and schizophrenia is tenable, phenothiazines are to be regarded not as mere tranquilizers providing only symptomatic relief, but as counteracting neurochemically the schizophrenic process itself.

Following the discovery of genetic markers for manic-depressive psychosis in color blindness and the Hg blood group, Wyatt et al (31) proposed that monoamine oxidase may similarly serve as a genetic marker for schizophrenia. This substance is markedly reduced in the platelets of schizophrenics and is also found in reduced quantity in the non-schizophrenic member of pairs of monozygotic twins discordant for schizophrenia.

While much remains to be done in unraveling the role of the internal environment in the causation of schizophrenia, the outlook has never been brighter.

Neurophysiological Model

Since the birth of the concept of dementia praecox and its subsequent transformation into schizophrenia, the underlying basis for determining the presence of this disorder has inhered in the contrast between a sound sensorium and an unsound mind, i.e., the presence of thought disorder, ambivalence, loose association, and so forth, in a person whose sensory and perceptual capacities are intact. This dictum has gone unchallenged for almost a century and has dissuaded many experimental psychologists from examining the psychophysiological, sensory, and perceptual functioning of schizophrenics.

More recently, it has become quite clear that the physiological and sensory functioning of the schizophrenic is not as free of deviations as had been thought. Crude global tests and techniques have always yielded differences between schizophrenics and normals to the detriment of the former, but such differences could usually be attributed to such global factors as lack of attention, motivation, etc. The more sophisticated and well-controlled the techniques became (e.g., choice reaction time, perceptual constancy, size constancy, etc.) the smaller became the differences, until they finally disappeared when attention was paid to the obvious sources of poorer performance—motivation, attention, difficulty of task, etc.

Recently, however, a group of techniques has emerged which seems to find differences between schizophrenics and non-schizophrenic patients and normals which will not go away under the most exacting controlled conditions. To be sure, the differences are not as dramatic as those found with the more global, uncontrolled techniques, but they are nevertheless real and must be dealt with.

These differences have emerged because of two developments. First, the global diagnosis of schizophrenia and depression and
personality disorders, based upon free-floating interview techniques, has been replaced in some laboratories by more objective systematic interviews which support the clinical diagnoses with a dimensional profile revealing the underlying psychopathology that characterizes the patient. And, second, an advance has come from progress in the field of physiological sensory and perceptual techniques which provide brief stimuli that elicit responses within the first 1,000 milliseconds. Such techniques are usually somewhat freer than the older techniques from the influence of motivation, prior learning and experience, etc.—in other words, from cultural adhesions to the task. Among these are certain types of reaction time experiments, temporal energy integration, auditory interaction of successive sound stimuli, and evoked potentials, to cite only a few.

To test whether the schizophrenic processes information through his central nervous system differently than the normal does, without involving the complications that ordinarily beset clinical testing, the task must be very simple. One task that can serve this purpose is simple reaction time, such as lifting the finger when a stimulus appears. Secondly, it should, if possible, be a task in which the schizophrenic “excels” the normal; otherwise, poorer performance could be blamed on lack of motivation. Third, it should reflect sensory or perceptual processes and not attitudinal factors. One source of attitudinal bias is eliminated by using forced-choice methods in which the subject must indicate which one of three stimuli is the odd one, reducing the degree to which differences found between schizophrenics and normal might be a reflection of their willingness to take risks in making a judgment. When the forced-choice method was used, Critical Flicker Fusion (CFF) failed to differentiate schizophrenics from normals, while the other psychophysical methods claimed that schizophrenics had higher thresholds (lower cps). On examining CFF by means of signal detection theory techniques in which sensitivity is separated from attitudinal criteria, it became clear that schizophrenics were not less sensitive, but more cautious; they required a lower rate of alternation of the light before they would be willing to judge the stimulus as flickering (38).

The following techniques from our Psychophysiology laboratories headed by Dr. Samuel Sutton (39) found schizophrenics to differ from, and in some instances even excel, the performances of normals and non-schizophrenic patients.

1. Critical duration

The Bunsen-Roscoe law states that up to a specified critical duration, intensity and time are interchangeable so that a bright stimulus acting for a few milliseconds will produce the same response as a less bright stimulus acting for a longer period, provided the total energy (product of intensity and time) remains constant. When the critical duration is passed, not all the energy of the stimulus is integrated and consequently some of it gets “lost” and does not affect the response. It is as if the cup of energy runs over when the critical duration is past, and the excess energy drains off. Consequently, reaction time which is inversely related to energy remains constant during the critical duration period since the total energy is integrated, but increases when the critical duration is surpassed since now there is less effective energy in the stimulus.

As a result of some preliminary investigations by Sutton (39), it was hypothesized that the critical duration for schizophrenic patients for light pulses was approximately 4-6 mscs, considerably shorter than for non-schizophrenic patients and schizophrenic patients, non-schizophrenic patients, and normals were compared by Collins (40) for their reaction time to a 4 msc pulse of light and a 6 msc pulse of light when both pulses contained the same amount of energy. The 6 msc pulse contained normals. In order to verify this preliminary finding, a group of two pulses of 2 msc each separated by a 2 msc dark period. This dark interval is well below the perceptual threshold so that the two stimuli were perceived as continuous by all the subjects.
The results vindicated Dr. Sutton's preliminary findings. The critical duration for the schizophrenic group was indeed shorter than for the non-schizophrenics and normals. The schizophrenics showed an increase in their reaction time to the 6 msec pulse, while the reaction time of the normals and non-schizophrenics was unchanged. Since 3 of the 10 patients in the schizophrenic group differed from their peers by not showing a significant increase to the 6 msec pulse, an examination of their other characteristics was undertaken. They were quite similar to their schizophrenic peers except for one factor—they showed little or no speech disorganization as measured by a systematic structured interview which was administered to patients and normals alike. In contrast, 6 of the 7 schizophrenics who raised their reaction time to the 6 msec pulse showed high scores on the dimension of speech disorganization, a factor which probably reflects thought disorder. It should be noted that this difference between schizophrenics and others cannot be blamed on lack of motivation or interest on the part of the speech-disordered schizophrenics, for they are, in fact, sensitive to a difference in the stimulus which escapes the normals and their schizophrenic and non-schizophrenic peers. No amount of effort in trying to get normals to sense the difference has succeeded thus far.

After refining our measures of speech disorganization and applying them to a new group of patients, we plan to apply the laboratory technique again to the new group to see how our initial finding holds up, hoping to be able to clarify our classification problem and obtain more homogeneous groups.

2. Reaction time to shift in sensory modality

Ever since Shakow's finding on the effect of duration of foreperiod on reaction time, which he reported in his Dean Award Lecture (34), we have wondered whether the observed effect is due to the difference between schizophrenics and normals in time judgment, an area so well studied by Lhamon and Goldstone (41), or whether it is a reflection of segmental set—the inability of the schizophrenic to maintain a set. Our own work in this area may cast light on this question. Instead of varying foreperiods, we varied stimuli—light and sound—and noted that when similar stimuli follow each other (ipsimodal stimuli) reaction time tends to decrease, but when different stimuli follow each other (crossmodal stimuli), reaction time increases. This effect is much greater in schizophrenics than in normals and the difference between schizophrenics and normals is enhanced when the guess that the subject has made of the identity of the stimulus, before it is presented, turns out to be right rather than wrong.

To explain this phenomenon, we first resorted to Shakow's set hypothesis that the patient may expect one of the stimuli; if the other is presented instead, it may take longer for him to react. To test this, we told the subject beforehand what the next stimulus would be, and verified that he correctly placed his finger on the button representing the modality of the next stimulus. Here there was no uncertainty, and a definite set compatible with the imminent stimulus was established.

Yet a greater retardation due to the modality shift persisted in the reaction time of schizophrenics as compared to normals. Apparently the shift in modality, regardless of the compatibility of the set, produced the retardation.

We then went on to examine Shakow's data more carefully (42) and found that when two identical foreperiods succeed each other, the reaction time to the second is not changed, but when two foreperiods of different duration succeed each other, the reaction time increases. Thus, if we view the foreperiod and the succeeding stimulus as a pattern, we can regard two successive identical foreperiod-stimulus combinations as if they were ipsimodal (ipsitemporal) in nature and two successive non-identical foreperiod-stimulus combinations as crossmodal (heterotemporal), and find longer latency in the latter case.
3. Auditory findings

The long-held claim that the auditory threshold of mental patients is no different from that of normals can no longer be accepted. Bruder, Sutton, Babkoff, Gurland, Yozawitz and Fleiss* have demonstrated that the threshold is higher in manic-depressives and, here again, the use of forced-choice and signal detection theory methods eliminates the possibility that lack of motivation is the cause of the difference.

Addressing a somewhat different question, the authors presented randomly either a click which was 25 decibels (db) above each subject's absolute threshold, followed 15 milliseconds later by a click which was 10 decibels above the subject's absolute threshold, or the more intense 25 decibel click by itself. Subjects were to lift their finger from a key as rapidly as possible on the presentation of either stimulus package.

They found that the average reaction time for normals to the paired clicks, the 25 followed by the 10, was only very slightly faster than the average reaction time to the 25 db click by itself. However, for the manic-depressive patients, there was a much larger improvement in reaction time for the paired clicks than for the single intense click presented by itself. Here, then, we have evidence that the patients were benefiting more from the presence of the 10 db click than were the normals. The manic-depressive patients are in this sense more "sensitive" to the presence of the 10 db click and in that sense performing better.

These manic-depressive patients were part of the U.S. sample in the U.S.-U.K. study (43,13) who were originally diagnosed as schizophrenic by their local state hospital clinicians, but were found to be manic-depressive by the project team. The inclusion of their data in a paper devoted to schizophrenia is indicative of the difficulties produced by inadequate diagnostic procedures. The patients who were diagnosed as schizophrenics by the project team did not differ from normals in their performance on the auditory tasks.

4. Comparison of evoked potential and reaction time results

When our Unit became disenchanted with the available clinical psychological tests because of their dependence on motivation, attention, and interest, as well as because of their lack of independent contribution to diagnosis and their failure in prognosis as Windle (44) pointed out, we turned our attention to the classic categories of human behavioral responses: physiological, sensory, perceptual, psychomotor, and conceptual, and devised a Mendelejeff-like table for classifying these five types of responses according to the kinds of stimuli that can evoke them (45).

These stimuli could vary from the idling state, when no stimulus was presented, to energy stimuli in which the response reflected the intensity of the stimulus, to signal stimuli in which the response depended more on the acquired or inborn significance or meaning of the stimulus. We tried to devise specific experimental situations in which each type of stimulus would elicit the specified category of response. More recently, we gave up this heterogeneous approach and decided instead to utilize the same type of response but elicit it by the different types of stimuli. We selected the physiological response as the "carrier wave" on which to impose the energy and signal loads and noted the variation produced in the response, selecting the evoked potential as one of our measures. We similarly chose reaction time as another measure of the effect of energy and signal types of stimuli. Our plan was to see whether the patterning of the evoked potential and of the reaction time responses to these stimuli would differentiate schizophrenics from other mentally ill persons and normals.

While it is quite clear that not all the rubrics in our grand design will show differences between the mentally disordered and normals, it is likely that the patterning of the responses...
across the rubrics may yield interesting differential data. Since each of these processes can be detected in the evoked potential, the effect of various cognitive factors such as uncertainty on the average evoked potential can be noted. We have found that some evoked potential components behave differently in schizophrenics as compared to normals and depressives.

Similarly, we can regard the psychomotor response in reaction time as a measuring device for the various loads imposed on the physiological response since it is a less demanding task than those which some of the other psychophysical tasks impose. It might be interesting to compare the influence of some of the cognitive loads on both the purely physiological response—the evoked potential—and the psychomotor response—reaction time. As will be noted from Figure 4 (46) the different loads seem to influence changes in contrary directions when schizophrenics and normals are compared.

When the state of certainty (knowledge of which stimulus is to be presented is given beforehand) is compared with that of uncertainty (no foreknowledge), the schizophrenic shows the greater change in reaction time, but the normal shows the greater change in average evoked potential. Similarly, having guessed correctly rather than incorrectly affects reaction time more in the schizophrenics, but affects average evoked potential more in the normal. Modality switch (when the stimulus shifts from one modality to the other) also affects reaction time more in the schizophrenic, but affects average evoked potentials more in the normals. Thus, the average evoked potential is more sensitive to changes in the normal in response to the cognitive load of uncertainty, guessing correctly, or shift in stimulus modality while these same cognitive states seem to produce greater changes in the reaction time of the schizophrenic. While this may appear as a paradox, empirically speaking, it provides us with an unexpected patterning that helps to differentiate schizophrenics from normals even more than if the changes went in

**Figure 4**

Comparison of Reaction Time Data and Evoked Potential Data on Contrasted Schizophrenics, Depressives, and Normals.

- **Top panel:**
  - C = certain
  - U = uncertain
- **Middle panel:**
  - R = right
  - W = wrong
- **Bottom panel:**
  - I = ipsimodal
  - C = crossmodal

the same direction. Perhaps simultaneous recording in the same patient of his reaction time and averaged evoked potential (which we are now doing) will cast even more light on the nature of the observed differential pattern and lead to fractionation of the global heterogeneous schizophrenic group into homogeneous subgroups.

Thus, we have shown that the sensorium of the schizophrenics is not as similar to the sensorium of normals as had been thought.

Therapeutic Intervention

An evaluation of therapeutic intervention requires us to consider whether each of the models we have described dictates the most useful kind of therapy based on the assumed etiology.

The ecological model stipulates that the sources of schizophrenia are to be sought in the ecological niche that the patient occupies in society, and that the causes are the stresses produced by that condition. For example, Cassel (46a) has claimed that the maldistribution of wealth and opportunity and the lack of public health care are causal factors in the high rate of schizophrenia in a rural county of South Carolina.

One of the current approaches to the treatment of schizophrenia based on ecological considerations emanates from the existential-phenomenological view of schizophrenia. Essentially, in its current form it stresses that schizophrenia is a life style and that the best way to treat it is to let it bloom unhampered and even encouraged. By living through his episode, the schizophrenic can gain strength to tide him over the psychotic break and benefit from it as a growth experience. The therapist’s function is to be a coequal partner in struggling through the episode rather than a superior dispenser of therapy.

An interesting example of the application of an existential-phenomenological approach is Soteria House (47), modeled to some extent after Laing’s (48) Kingsley Hall. One wonders, however, whether there is a way of transferring the modified behavior developed in such places as Soteria House to life outside. Fortunately, Soteria House has provided a systematic description of the kinds of therapeutic endeavors that are applied and a suitable conceived control group, together with a cluster of suitable techniques for measuring the outcome. The results of a current study comparing Soteria patients to those of a community mental health center are being looked to with great anticipation.

The developmental model stipulates that the sources of schizophrenia are to be sought in the transition of man from one stage of development to the next. When the supplies, nutrition, and support required for helping in the transition from one stage to the next are missing or are inadequate, schizophrenia may develop.

What type of therapy is dictated by the developmental model? The recent work in mother-neonate interaction seems to hold out promise for therapeutic intervention. The powerful effect of reinforcement during nursing on the neonate, eye-to-eye contact between mother and child, the possibility of superstitious behavior tendencies arising from the inadvertent reinforcing effect of the nursing act on any or all ongoing behavior, and expectancies which may by chance lead to aggression, submission, dependency, etc., open up new possibilities for investigation. Perhaps these contingencies are so important for subsequent development that we should make them a major focus of our research and clinical efforts.

The learning theory model would lead us to adopt behavior modification methods on the assumption that there is no underlying disorder. Deviant behavior itself, be it phobic depression, psychosomatic, or what not, becomes the target to be eliminated by behavior modification methods.

Certain implications from our models might indeed lead one to engage in the development of behavioral prosthetics for schizophrenia. If we accept Salzinger’s immediacy hypothesis, we might develop tape recorders to allow the particular message
to be played back in its entirety so that the attention of the schizophrenic would be called to the long-range aspects of the message. In that way he would overcome his fixation on the immediate aspects of his environment. Or perhaps speeding up the message would tend to bring the fullness of the communication into better perspective.

One of the prosthetic devices utilized to improve ward behavior of schizophrenics is a token-economy system in which good performance is immediately rewarded with a token which can be bartered for certain privileges. This system seems to improve ward behavior considerably, often, however, without affecting other aspects of psychopathology or without transfer value to extra-ward behavior. It is not clear what bearing this latter fact has on the validity of the learning theory model. It may be that the therapy treats only peripheral aspects of the total illness picture, or, on the other hand, the therapy may indeed be directed at the core process, but fail to yield permanent results because conditioning techniques are lacking for transferring the effects of behavior modification from the ward into wider social contexts.

The internal environment model would stipulate that somatic and psychopharmacologic methods are the answer. This model has perhaps made the greatest demonstrable advances in the last few decades. The whole armamentarium of psychopharmacology has been turned loose on schizophrenia. While it is generally agreed that we have not yet found the biochemical basis for schizophrenia, we have succeeded in mitigating the condition by the use of drugs. Whether chemotherapy in itself is sufficient or whether it needs the support of psychotherapy or other psychological aids is still not finally answered. May (49) has recently shown, however, that chemotherapy without the aid of psychological intervention seems to do better than psychotherapy without the aid of chemotherapy.

No therapy has as yet been directed at the neurophysiological model, and yet biofeedback experiments may teach us how to control and perhaps abort the neurophysiological substrate of anxiety, depression, and thought disorder.

If we accept Venables's (50) hypothesis that the arousal level of the schizophrenic is different from that of the normal, it may be advisable to train the schizophrenic to lower his arousal level by means of biofeedback. Another possibility is to take the generally slower reaction time of the schizophrenic patient into consideration and deal with him in a way which would compensate for the slowness.

**Model for Therapeutic Intervention**

In searching for a model for therapeutic intervention, I harked back to the literature on prognosis. This literature is rather vast and varied. I had surveyed it in the early 50's in connection with our prognostic study. The one outstanding effect of this survey was to make us realize that in most cases, long before the disorder struck, the future patient had a personality, a style of life, a degree of adjustment, usually overlooked, which was an important determiner of the change in behavior (illness) which the onset of a disorder produced. No two schizophrenics look alike. In their case, not only are we ignorant of the focus of the disorder, but its interaction with the premorbid personality and the ecological niche so colors the resulting illness that similarities between two schizophrenics' behavior may be far less than the differences they exhibit. But premorbid personality and the ecological niche not only determine the illness—the immediate response to the disorder—they also largely determine eventual outcome.

If I were to summarize the results of our prognostic review in one phrase, it would be that the best predictor of outcome is the premorbid personality. In trying to fathom why the premorbid personality plays such an important role in determining outcome, I have proposed the following model for therapeutic intervention.

Let us assume that the schizophrenic is a vulnerable personal-
ility who, when subjected to sufficient stress, will be catapulted into an episode. Let us further assume that all episodes are time-limited and that when the episode ends, the patient returns to his premorbid level or close to it. If he had a good premorbid level to begin with, he returns to his premorbid status in society and is regarded as recovered or at least improved. If his premorbid level was poor, what has he got to return to? He could hardly cope before he was catapulted into the episode and he still cannot cope when the episode is ended. As a matter of fact, it is difficult to determine in his case when the episode ends.

We might go a step further, somewhat beyond our data, and assume that all schizophrenics recover from their episodes. What we call chronic schizophrenia would represent a category of individuals who are no longer suffering an episode, but who appear to be still sick because the premorbid personality to which they have returned is not sufficiently well developed to enable them to cope. Furthermore, the hospital stay often teaches them the patient role so well that they develop what Gruenberg (51) has dubbed the SDB—social breakdown syndrome.

The number of such patients is not inconsiderable. Before 1930 and the advent of the shock therapies and the more recent chemotherapies, about one-third of the schizophrenic admissions got out and stayed out, about one-third oscillated back and forth in the hospital, and the remaining third stayed permanently in the hospital (52). Currently, we have continued to release the first third; the middle third, with the help of drugs and other interventions, also generally stays out longer; the last third has become the oscillating group because of its poor premorbid status. It is the last group that needs the special intervention I am discussing here.

One might go still another step further and say, don't bother so much about treating the good premorbidss—they'll get well anyhow or will get well quicker with suitable intervention. Concentrate on the poor premorbidss and utilize whatever therapeut...
based on his own self-assessment; second, the assessment of the therapist; third, the opinion of the family; fourth, the attitude of society as a whole; and fifth, the burden or lack of it which the system of delivery of care has to bear with regard to the former patients. Each of these ways of assessing outcome of illness is biased in the interests of the agent doing the evaluation, and these five ways of assessing outcome are not very highly correlated. The problem, then, becomes one of choosing the best set of weights for combining the five different assessments, or finding an independent measure that will be free of bias.

Several tools have been developed for assessing outcome on the basis of these criteria. The self-evaluation of the patient can be obtained on a set of self-reporting inventories such as the MMPI. The evaluation of the therapist can be obtained by means of a technique developed by Gurian (53, 54) known as the SSIAM, and the systematic structured interview used in diagnosis can be repeated to determine what changes have occurred on follow-up in the psychopathology of the patient. Special measures like the Katz Adjustment Scale (55) can be administered to family members to determine their evaluation of the patient.

The evaluation of the former patient by society, with regard to his reintegration into the social structure, is now being accomplished clinically by sensitive social workers, and attempts at determining his level of coping have been provided by social scientists.

Finally, the degree to which the system of delivery of services gets involved with the patient after his discharge can be measured by outcome indices such as suggested by Burdick (56), in which the proportion of time spent in the hospital after first admission is considered in relation to the ratio of number of discharges to readmissions during the follow-up period. The product of these two factors varies from near zero for the best outcome index to 1.00 for the worst outcome. Those with a zero index enter the hospital for a brief time and never return, while those who achieve an index of 1.00 remain in the hospital continuously.

No one has ever tried to integrate these five measures of outcome into a composite. Perhaps it cannot be done successfully. On the other hand, even if these criteria are not summative, it is possible to utilize typological approaches which would classify individuals into subtypes in accordance with the pattern presented by their status on the five criteria, giving us, once and for all, a systematic structure for assessing outcome.

Summary

What does all this mean? First of all, one can raise the question, as Dubos (57) has done, whether all of our scientific findings have any significance for the human condition—and specifically, have they any significance for the human condition known as schizophrenia?

Thus far we have described the etiological models as blind forces which control man's destiny; to some extent, given the current scene, it is a true picture. For the ecological niche in which man finds himself does determine his well-being, his genetic makeup does limit his potential, his developmental past and learned behavior do confine his future, his internal environment and neurophysiological makeup do control his behavior. And, in fact, we might agree with Dubos that all of these forces are merely the "stage props" for the drama that man is to enact on the stage of life. However, we have left out perhaps the most important determinant of man's stage behavior—his ability to be a self starter, to alter developmental trends, to modify his internal environment as well as his neurophysiological equipment. Unlike other organisms which are shaped by their environment through eons of gradual evolutionary developments, man can shape his own environment if he chooses to
do so and has developed the know-how to apply changes not only to the exogenous but also to the endogenous environment. It is in these directions that the future of man's normal development, as well as the containment and improvement of abnormal development, lies. And it need not take eons to accomplish, for we can produce changes for the better even in our own lives and in our own lifetimes (20a).

Meantime, despite the fact that all we now understand and thus are able to control are the mere underpinnings of the stage on which the dramatic action takes place, we still may hope to control the form if not the content of the action. Perhaps the underpinnings of tragedies like schizophrenia are different from the underpinnings of comedies. Perhaps the simple differences which differentiate the schizophrenic—his inability to shift as readily, his shorter critical duration, his lower amplitudes in evoked potentials, and the different patterns produced psychomotorically, as contrasted with perception under the influence of uncertainty, reward, punishment, etc.—constitute the real building blocks of schizophrenia. He begins to feel different and appears to his friends to be different because of the small discrepancies in his behavior. Once these differences become recognized by him and by his peers, the rest of schizophrenia begins to develop. In other words, schizophrenia is "caused" by these small losses of pawns in the game of life—the rest of schizophrenia is merely an epiphenomenon. I realize that this is a highly controversial point of view, but this is what I have come to believe is a possible, though not yet probable, explanation of some types of schizophrenia. In short, schizophrenia occurs in a vulnerable individual when he is subjected to sufficient stressors—and his vulnerability is detectable in the differential patterns of his central nervous system responses. How to manage this vulnerability and protect the individual from succumbing to the disorder are the challenges which this model places before us.
A BIOMETRIC APPROACH TO DIAGNOSIS


