Scientific Models for Psychopathology in the 1970's

By Joseph Zubin, Ph.D.

Most of us past 50 can recall the days before the advent of the drug revolution when custodial care was the mode, psychosurgery was in bloom, electroshock treatment (ECT) flourished, and insulin was in flower. Those were heroic days, life seemed simpler; diagnosis was unnecessary, psychotherapy was in doubt, and psychoanalysis very rewarding, at least to analysts. Our hospitals were overcrowded, community psychiatry not even a pipe dream, and sensitivity training unheard of. The air was still clean, our language still pure, our noise level bearable, our youths still tractable, and women still unliberated. With the advent of the drug era, all hell broke loose! The air became dirty, language foul, noise level unbearable, youth impossible, psychoanalysis declined, diagnosis again became necessary because our choice of therapies multiplied, our hospitals began to empty, and our entire environment and culture became threatened by pollution. Yet, there seems to be a balance in nature—a law of conservation of pollution—for, when our air and language were clean, noise level low, and drugs were still medicine, sex was a dirty word, and now, with sex clean . . .

While psychopathology was undergoing these tremendous upheavals, it became more and more difficult for us in the clinics and laboratories to maintain our equilibrium and hold on to some schemas which could render our work meaningful. I entered psychology when psychometrics was in its heyday and soon became interested in personality. I weathered the waves of factor analysis, psychoanalysis, and projective techniques as they swept over personality measurement, and searched each movement for some guide to deeper understanding of the mainsprings of personality and its deviations. I found these movements either too static, too dynamic, or too unreliable and invalid, respectively. Together, with the late Carney Landis, I even tried the effect of antihistamines on personality measurement before the current drug era began.12

This was, no doubt, stimulated by Kraepelin's early attempts at utilizing drugs in psychopathology. Realizing that, at least, modern personality theory arose historically out of psychopathology, I turned my attention to abnormal psychology and began a career of teaching and research in which I have remained for the last 40 years or so. It was my teaching that gave me the most trouble! I could carry on experiments with mental patients without too much difficulty and with some exciting results, but my students kept on demanding some rationale for what I was doing. Using curiosity as a guide for research seemed unacceptable, for there were too many things to be curious about, and how does one select from the plethora of possibilities? What framework was there for integrating the new findings? Or were they to remain isolated findings without reference to the accumulated knowledge of the work of others? Furthermore, genetics and biochemistry, fields of which I was ignorant, were demanding attention, and I had to do some fast reading to keep ahead of my students. This is when I turned to reading philosophy of science and where, through the works of Reichenbach, I finally began to realize the need for scientific models as guides for my work. Perhaps the clearest introduction to this point of view was the one I found in Kaplan's systematic presentation of scientific models.11

There have been many divergent uses of the concept of model, which ranges from small-scale mechanical models of the type that the United States Patent Office used to
require for each new invention, to abstract mathematical models that transcend the substantive material they deal with. To avoid any confusion, let me define scientific model.

A model is a reconstruction of nature for the purpose of studying a given phenomenon. It is built by a process of abstraction, defining a parsimonious set of parameters that are intended to leave intact the essential aspects of reality, while removing distracting elements. It may be necessary to introduce certain patently unreal assumptions in order to make the investigation of the phenomenon possible, e.g., assumption that mass is concentrated at the center of bodies, a patently unreal assumption which, nevertheless, made Newton’s model of gravity possible. Examples more relevant to our field are the assumption of continuity in distribution of data which are, by necessity, discrete or the assumption of a normal distribution in a variable which patently does not satisfy the normal distribution curve and which must be transformed to meet the assumption. These models give rise to hypotheses that can then be probed for their tenability through direct observation of nature. The purpose of models is, therefore, to improve on nature by simplifying it in order to engender further research in a systematic way and thus add to the body of scientific certitude. There are those, however, who eschew scientific models and instead prefer to confront nature, with all its vicissitudes, directly without interposing the screen of simplification which scientific models attempt to provide. As Blackburn² noted, the alternative to the conventional scientific approach is the sensuous approach which stipulates that “there is other knowledge besides quantitative knowledge and there are other ways of knowing besides reading the position of a pointer on a scale.”

He goes on to say that the sensuous and the objective approaches show a complementarity similar to that shown by the wave and particle theories of light. Both deal with the same phenomenon, yet produce different views of their nature and indicate the essential dependence of our observations on the tools we use for making them. “Thus one can predict rain by reading the barometer, or by going outdoors and sniffing the air, or noting a sudden increase in rheumatic pain in his joints with about equal reliability!”² I dwell on this point because many of my clinical research friends have impressed me with their belief in the sensuous or, as we call it, the phenomenological approach to psychopathology. I believe they have a point which other scientists sometimes overlook, since neither phenomenological nor quantitative knowledge of nature is complete in itself. Both Newton and Goethe, for example, were right regarding the nature of color and the complementarity of physics and art. Yet there is a difference between the phenomenological and scientific view which should not be overlooked. Science deals with public events while phenomenology deals with the still private events. In my own thinking, I have often likened our own biometric approach to the holding up of a mirror to the phenomena under investigation, capturing a mirror image of what the phenomenologist perceives and, in this way, making it available to the view of others besides himself. But it is only an image the phenomenologist would say, not the real thing that he perceives, and it captures only part of the phenomenon, overlooking what is still shrouded in darkness. However, let us not forget that the phenomenologist’s reality is also only a model. What the mirror image captures for the scientist, however, becomes a public event subject to the scrutiny of others.

Psychopathology is rich in phenomenology and there are any number of systems for classifying and diagnosing the observations made on patients. However, when it comes
to etiology, our ignorance is abysmal. What does one do when faced with such total ignorance? The only thing left to do is to imagine “as if” causes and test them. But to describe an etiologic model as an “as if” cause does not do full justice to the concept—a good, creative etiological model is based on a daring idea about reality entertained playfully for the pleasure it affords as well as for the research it engenders. The distinction between the possible and the impossible is consciously suspended momentarily. The idea is implicitly introduced by, “Wouldn’t it be funny if...” This type of model probably represents the highest level of scientific maturity of which man is capable.

In developing such models, it is important to bear in mind that one can sometimes find a circumscribed model that will satisfy a given set of conditions but will not add to understanding causes. Thus, models can be constructed which will predict the tides rather accurately for a decade or so, but which have no value for explaining the causes producing the tides. Such mechanical models may be of extreme immediate value economically or socially but are of little value in scientific understanding of the causes of phenomena. The amphetamine model for psychosis may be a case in point and, despite its usefulness in clarifying dopamine-norepinephrine relationships to behavior, it may divert us from the basic search for etiology of schizophrenia, since it is an analogous rather than a homologous model.

What models have served psychopathology in the past? Historically, scientific models reflect the zeitgeist rather closely. Thus, when primitive religion held sway, demonology served to explain psychopathology; when astrology reigned supreme, the stars affected the humors of the body to produce psychopathology; and when Descartes’s machine models were popular, defects in hydraulic pumps or in watchmakers’ models of human beings served as the paradigms of psychopathology.

When the brain began to be regarded as the organ of the mind at the turn of the century, brain anatomy was searched for the cause of mental disorder giving rise to neuropathology as one of the first scientific endeavors in psychopathology. Thousands of postmortem brains were sacrificed to the search of the never-present lesion. More recently, with the rise of bacteriology, models provided by the infectious diseases held sway, giving rise on the positive side to the conquest of general paresis and on the negative side to Henry Cotton’s focal infection theory and to Lowenstein’s implication of the tubercle bacillus in schizophrenia. There soon followed the biochemical and genetic models for mental disorder in the wake of the discovery of inborn errors of metabolism. Finally, with the advent of the information and communication theory, brain models again came to the fore, but this time, not as anatomic models, but as data-processing models. One of the popular current models for the brain is that of a computer with psychopathology resulting when the computer is overloaded or otherwise interfered with.

It should be remembered that the brain has only a limited number of responses, but the stimuli that can produce a given response are well-nigh infinite. That is why a given effect can not be assumed to be related to only one type of stimulus or cause. However, psychopathology is an ancient craft and has adjusted to all kinds of invasions of its domain. We have lived with primitive religion, medicine men, alchemists, astrologers, early anatomists, phrenologists, theologians, philosophers; in modern times we have had commerce with neuropsychologists, physiologists, psychologists, psychoanalysts, neurologists, geneticists, biochemists, neurochemists, biologists, and social
scientists—and finally even with psychiatrists. The decade of the 1950s belonged to biochemistry, that of the 1960s will certainly mark psychopathology’s communion with neuropsychopharmacology and the late sixties and early seventies its flirtation with biometrics. Psychopathology can live with all of these, it welcomes them, and will eventually domesticate them. It will absorb them, even as ancient China absorbed all its invaders. Eventually, they will all have enriched psychopathology by their impact and a balanced science will emerge in which their residues will become distinguishable only historically as is the case with the residue left by Anglo-Saxon, Latin, and Norman-French in modern English.

What are the scientific models that are now occupying the area of psychopathology, and what are their accomplishments?

I have elsewhere described these models in great detail. Here let me briefly review them for you and indicate the nature of their contributions. First, we must draw a distinction between descriptive approaches and etiologic models. We have now had 34 centuries of description dating back to the sacred Hindu sources of the Ayure-Veda and to some of the most incisive delineations of psychopathology through the literary efforts of the world’s great writers and poets. However, description never cured anyone, nor did it throw light on causes, but it did help define the field of inquiry. We are now cashing in on the multiplicity of observations of mental deviation through the centuries by systematizing them, through the use of structured interviews, and by developing dimensions for depicting the behavior of the mentally disordered in objective, reliable, and often valid fashion. This has been hastened by the demands made by neuropsychopharmacology for measuring the behavioral changes that accompany drug treatment. We now have a variety of systematic interviews which have been factor analyzed and computerized so that soon after completing the interview we can provide dimensional profiles as well as computerized diagnoses. These approaches have already paid off in the following ways: First, the much debated differences in hospitalized mental disorder between the United States and United Kingdom have been found by our objective systematic approaches to be reflections of differences in psychiatric rather than national cultures. Furthermore, because of the looser relationship between diagnostic categories and psychopathology in the New York than in the London mental hospitals many more New York patients fail to receive proper treatment for depression and mania than is the case in London. With the help of the newly derived dimensions of psychopathology it has become possible to demonstrate quantitative differences between neurotic and psychotic depression, between schizoaffective and other types of schizophrenia and between various other diagnostic groupings. Furthermore, the elimination of target symptoms at which drugs aim and the development of new drugs for specific targets became possible only when systematic objective interviewing and rating techniques became available for determining the presence of the symptomatic behavior and its alteration after treatment.

When it comes to the etiologic models, we have not made as much progress yet. In the few instances where the etiology of a disorder was discovered, as was the case with general paresis, pellagra with psychosis, phenylketonuria (PKU), galactosemia, Down's syndrome, and other types of mental retardation, the disorders either disappeared or were taken over by other disciplines, leaving only the disorders of unknown origin for psychopathology. Nevertheless, even at the risk of sawing off the very limb we stand
on, we must provide, if not demonstrable causes, at least presumed causes in the form of models.

It is too late in the age to try to reduce etiology to a unidimensional framework such as that provided by genetics or ecology, since the evidence is so clear that multiple etiology will be found to be the rule rather than the exception. Nevertheless, it is important to push each unidimensional model as far as we can, before inquiring into its interaction with other models. We are somewhat in the same position as a statistician faced with a problem in the analysis of variance. He knows full well that none of his main effects operate independently and is fully aware that he must look at their interactions, but before he can do so, he must first separate the main primary effects. This is how we will proceed. We will formulate each one of our models independently and then look for their interactions.

There are six such models now in the field: The ecological, developmental, learning and conditioning, hereditary, internal environment, and neurophysiologic.

The ecological model simply stated assumes that the sources of man’s mental disorders are to be sought in the characteristics of the ecological niche which he occupies and that all of us are vulnerable to noxious niches. According to this model, the ecological forces impinging on the niche determine the particular nodal point occupied by the individual and thus determine his behavior. Among the contributions of this model have been the establishment of the importance of such factors as population density and crowding, socioeconomic level, educational level, occupation, degree of neighborhood disorganization, minority or majority status in the community, degree of isolation, and similar ecological factors in the productions of not only mental disorders but also of physical disorders. Just how these factors bring about a mental disorder is still a moot question but from the point of view of the ecologist, the ubiquitous tubercle bacillus for example is no more important in the production of tuberculosis than the noxious environmental factors and emotional stress which make possible the proliferation of the tubercle into body organs (keeping genetics, development, learning, internal environment, and neurophysiology constant). All are necessary, but not sufficient if one or the other is missing. It is likely that mental disorders behave in similar fashion.

Thus, mental retardation in which there are no organic or genetic involvements, is an example of the influence of a noxious ecological niche preventing normal mental development, and leading often to irreversible psychopathology. On less persuasive grounds, Murphy has proposed that there might be an association between schizophrenia and being raised as a Catholic since regardless of ethnic origin, it is the Catholics in each of the ethnic groups in Canada that have higher first admission rates for schizophrenia than the non-Catholics in the same ethnic group. The fact that this conclusion is based on hospitalization studies rather than on population studies, makes the conclusion more tentative, yet it offers a challenge for further investigation. Unfortunately, we do not yet have a taxonomy of ecological factors which make systematic studies of communities possible. However, the recently developing studies of ecological psychology by Barker, social networks by Hammer et al., and others will no doubt bring about a clearer view of this taxonomic problem. Some of the accomplishments of this model have been the studies of the ecological bases for suicide dating back to Emile Durkheim’s original formulations, the role of isolation in the
production of schizophrenia and disorders of the senium, and the role of community disorganization in the production of schizophrenia.

The developmental model stipulates that the origin of mental disorders is to be sought in the transitional stages which man passes through as he develops from fertilized ovum to fetus, neonate, child, adolescent, adult, presenium, and senium stages. Should there be lacking any of the needed nutrients or supplies that are required in passing from one level to the next, or should noxious events intervene, e.g., toxemia of pregnancy, perinatal difficulties, fetal or neonatal anoxia, isolation and deprivation in childhood, the probability of mental disorder is increased. Thus, if there is insufficient protein available while the brain is developing, if there are no suitable peers to help the shift from family dependence to peer acceptance, if in passing from later adulthood to the senium he fails to make the proper gradual disengagement, he may be at high risk of mental disorder. Some of the studies based on this model have indicated that in animals, the absence of peer play is far more important than the absence of mothering in later psychosexual and personality development, and in humans, absence of intimacy with friends during adolescence characterizes those who later become schizophrenic. Some of these studies have indicated the role of noxious intrauterine experience in the development of subsequent psychopathology. The study of Pasamanick, for example, is a classic landmark in this area. A most ingenious, fantastic hypothesis emanating from the developmental model stipulates that autistic children develop precociously in utero and spend the critical period for early socialization—usually 15 months after fertilization of ovum—while still in the isolated confines of the intrauterine environment and become imprinted with this asocial milieu. Once this critical period is passed, they fail to develop speech and other social interactions because the process is no longer reversible under ordinary conditions.

The learning and conditioning model stipulates that one learns to become mentally ill even as he learns to become mentally well. According to the strict behavioral view, there is no need for assuming an underlying disorder which produces deviant behavior; instead the deviant behavior itself is the disorder and it is learned through experience, and not produced by an underlying disease. Since the abnormal behavior is learned, the usual methods of acquisition of normal behavior will describe the paths to abnormality.

Indeed, according to this model, many behaviors generally accepted as normal might well be labeled psychopathologic—by the community or even by the individual himself—if they occurred with markedly different frequency or intensity or on other than the typical or “acceptable” occasions. The development of behavior theory to the point where it can handle complex behavior patterns; the demonstration by Neal Miller and others of the modifiability of a host of internal processes by application of conditioning paradigms; the proliferation of biofeedback studies, e.g., alpha-wave conditioning—all of these point to the enormous range of possibilities for the development of psychopathology through elaboration of the basic laws of learning.

Of course, the large literature on the production of abnormal behavior in lower organisms has long since made such a view tenable. The literature also shows us that topographically similar behaviors may be produced by different means and thus be of different functional significance for the organism. To cite but one relatively simple example, so-called emotional behavior may be a consequence of the Pavlovian discrimi-
nation situation, pushed beyond the organism's ability to discriminate, of an extinction procedure (depending on what the previous reinforcement contingency was), or of direct shaping through selective reinforcement of any or all of the component behaviors. Thus, there is no compelling reason to assume that apparently similar behavior in different individuals was necessarily established in the same way in all cases. This underscores the need for a functional analysis, not simply a topographical description, of the behavior of interest, although it must be pointed out that such analyses typically must be concerned with the discriminative and reinforcing stimuli currently maintaining the behavior; the retrospective reconstruction of the conditions obtaining when the behavior began is almost always too imprecise except where the entire sequence is controlled in the laboratory.

There is obviously not enough space to review the extensive animal studies, in which we see how a wide range of variation in positive and negative reinforcement schedules and their combination can produce a variety of behaviors which we might label abnormal, although we must be careful not to equate abnormal with unlawful. The application of these learning paradigms may consistently result in their respective behaviors in question, even though the behaviors themselves look abnormal simply on the basis of topographic description. Two interesting examples are avoidance conditioning and so-called response suppression. Salzinger has pointed out that in avoidance behavior (in which, for example, the unconditioned aversive stimulus is a shock and the conditioned response is a bar press timed to postpone or prevent the shock), the aversive stimulus brings about its effect when it does not occur. In relating this to human behavior, it is interesting to note that stimuli which bring about their effect when they do not occur present great difficulties to an observer who is trying to uncover the etiology of the behavior. In the absence of knowledge of the history of the response, it will be difficult or impossible to discover what is controlling the response, and the behavior will thus appear very peculiar to the observer.

Animal analogies for depression are available in the conditioned emotional response. Analogues for mania have also been provided. Sidman et al. showed that when the conditioned suppression paradigm is superimposed upon behavior controlled by avoidance conditioning (e.g., pressing the bar every 20 seconds to avoid shock), the warning stimulus (preceding the aversive one) increases the rate of response rather than suppressing the response.

Among other phenomena which the learning theory model helps to elucidate are hallucinations, phobias, and aggression. Hefferline and Perera have conditioned subjects to respond to a subtle thumb twitch of which they are not even aware. When the experimenter made the occurrence of a tone contingent on the thumb twitch (detected only by the experimenter electromyographically) and then gradually diminished the tone's intensity, the subject still responded when only the thumb twitch occurred, and reported that the tone, which was in fact absent, was his signal for response. It is of interest to note that the subject reported the occurrence of two successive tones when the experimenter slightly delayed the actual tone after the thumb twitch. Apparently the subject could not discriminate between the hallucinated and real tone.

While for obvious reasons, it is not desirable to teach abnormal behavior to human subjects, Haughton and Ayllon did succeed in inducing and later eliminating a pur-
poseless and persistent symptom in a patient through systematic conditioning. This behavior apparently met all the clinical criteria of a real symptom and was repeatedly evaluated as such by persons not told of the experiment.

The sum of this discussion is that experimental findings from many sources lend weight to the learning model. We can expect, as researchers continue to develop increasingly sophisticated analyses of complex human behavior in learning theory terms, that the learning model of psychopathology will continue to gain in its influence.

We have covered the three scientific models which may be regarded as exogenous since ecology, development, and learning depend so much on the influence of external forces impinging on the behavior of the individual. Some difficulty may arise in distinguishing among these three exogenous models. The ecological model is primarily concerned with the forces that produce a complex balanced system of interlocking subsystems in the niche an individual occupies and which may lead to maladaptive behavior. A learning theorist regards the world as does an engineer, subject to his manipulative ingenuity, and psychopathology is the result of manipulations of the environment by a person or his family and others leading to maladaptive behavior. Development is separated from learning in the same way as ethology differs from experimental learning theory. The former approaches the problems of psychopathology naturalistically and intervenes experimentally only to determine the underpinning of development, while the latter regards schedules of reinforcement, reward, and punishment as the basic underpinnings of maladaptive behavior.

Perhaps the best contrast between the developmental and learning theory models is to be found in the contrast between Skinner's and Chomsky's views regarding language. While both have in common the need for some genetic inborn propensity for linguistic development, Skinner's approach is primarily a learning dependent theory in which selective reinforcement of the wired-in sound potentialities serves as the touchstone for speech and Chomsky's approach is essentially a developmental model relatively independent of acquired culture and more dependent on universal rules emanating from maturation rather than learning.

More bluntly, Chomskyan would say that reinforcement can no more explain language acquisition than knee-jerk conditioning could explain football while the Skinnerians would counter that generative grammar can no more explain language than the preformation hypothesis could explain development.

The hereditary model for the etiology of psychopathology is so well established in our midst as a result of the work of Rüdin's school, Kallmann's laboratory, and the more recent work of Slater, Shields, Kety, Rosenthal, Schulsinger, and Mednick, to name only a few, that I am not going to spend any time discussing its importance, except to point out as a challenge, rather than as a conviction that strictly speaking there are probably no genetic disorders nor any environmental disorders in our field. We designate a disorder as genetic when we are still ignorant of its environmental parameters and vice versa. In most so-called genetic disorders, the hereditary component is necessary but not sufficient for producing a disorder. Similarly, for most so-called environmental disorders, the noxious environmental parameters are necessary but not sufficient. It is the interaction of both hereditary and environmental factors that is both necessary and sufficient for producing a disorder. I can conceive of a genotype that could survive and maintain its health and prosper in the most in-
hospitable niche which our planet or any other planet can offer. By the same token I can conceive, at least in theory, of an ecological niche which could maintain the health and well-being of even the most deficient genotype who could hardly survive in the usual niches on our planet. It is true that inherited conditions like family amauratic idiocy (Tay-Sachs disease) or galactosemia lead inevitably to a disorder and early death, and hence, this disease might claim that its genetic loading alone is sufficient to produce the disorder. But let us not forget that, as in PKU, the environment may also play a part and it is at least conceivable that in some environments where the oxygen tension, air composition, and nutritional source differs, the propensity for Tay-Sachs disease or Huntington’s chorea (like the propensity for PKU in an environment free of phenylalanine or for galactosemia in a milk-free environment) would remain dormant.

Long ago Darwin and his followers pointed out the role of the ecological forces in gradually selecting for survival those individuals whose genetic endowment suited the niche and eliminating those whose genetic endowment was ill-suited. A similar selective process operates on the inborn behavioral repertoire of man. Here too, the ecological forces select for survival those behaviors which the niche reinforces and cast into oblivion those which go unreinforced or negatively reinforced. Unfortunately, some ecological niches tend to reinforce inborn behavioral tendencies which lead to psychopathology. In this way the gradual selective effect of reinforcement shapes both normal as well as abnormal individuals.

This principle of selective evolution under the pressure of the environmental forces even holds for the selection of ideas and models since only those which find reinforcement in society tend to survive and even useful ideas or concepts often have to bide their time in obscurity until they are rediscovered.

So far as the model for the internal environment is concerned it stipulates that the sources of mental disorder are to be sought in the interior milieu—in the metabolic and biochemical characteristics of the organism, its body fluids, enzymes, and metabolic products. However, we must remember that the biochemical agents, like the genetic, may be necessary but not sufficient.

We now come to the last model, the neurophysiologic model which, simply stated, stipulates that the sources of psychopathology are to be sought in deviations in brain function, especially the electrophysiologic aspects of its functioning. Grey Walter has described in this volume the important aspects of this field, especially in so far as contingent negative variation (CNV) is concerned. In our own laboratory we have been concerned more with the behavioral aspects of brain function with special reference to information processing. Our original hope had been that the sources of psychopathology could be mapped by examining the patterns of behavior which patients exhibit in the way they process information under psychological testing. The different patterns that such patients exhibit on these tests could then be used to objectively identify the various types of disorders, as Kraepelin has suggested.

To our great dismay, the various clinical psychologic tests ranging from intelligence to personality to projective tests were quite disappointing because they were so heavily dependent in many instances on the idiosyncratic reinforcement history of the individual as well as on his ecological niche. Even the Rorschach test turned out to be nothing more than an interview which, when analyzed for its content, yielded results comparable to those of other interviews which are so heavily determined by culture. Consequently, we turned to the classic response categories—the physiologic, sensory,
perceptual, psychomotor, and conceptual. To elicit such responses under controlled laboratory conditions we needed to classify the variety of stimulus situations that could be used and chose the following: (1) idling state (initial level of functioning with no stimulus load); (2) energy stimulus (in which the response reflected the energy input, rising and falling with the intensity of the stimulus); and (3) signal stimuli (in which the response depended more on its significance based on the prior reinforcement history of the organism with respect to the stimulus than on its energy level, e.g., the cry of "fire" would elicit a response far stronger than the cry of "mire"). Fortunately, the evoked potential could serve as the carrier wave for the five response classes. The level of arousal which looms so importantly could be gauged by the amplitude of the average evoked potential (AEP) before any stimulus is introduced. The early components N₁, P₁ of the AEP could be related to the sensory load imposed by an energy stimulus. The later components N₂, P₂, N₃, P₃ could be related to the perceptual, psychomotor, and conceptual loads imposed on the organism by suitable stimuli or stimulus situations. The patterns across these types of responses (physiologic, sensory, perceptual, psychomotor, and conceptual) could be used to classify individuals into like-minded subgroups characterized by similar patterns.

We have not yet reached the point where the entire pattern of responsiveness has been examined, but partial patterns have already been found to differentiate patients from normal subjects and, in some cases, between subgroups of patients. Thus, schizophrenics tend to show greater retardation in reaction time when the modality of stimulation is switched from light to sound or vice versa in studies conducted by Sutton.²¹ Schizophrenics who suffer from thought disorder tend to have shorter critical durations than other types of schizophrenics, depressives, and normals. In this experiment, the reaction time of the subject remains unchanged for varying complementary values of intensity and duration of the stimulus, so long as the total energy of the stimulus (product of intensity by duration) remains constant. This holds true for normals and depressives for durations as long as 13 msec for the particular intensity used in our laboratory, but when the duration exceeds this critical value, the total value of the energy fails to make itself felt and with this reduction in effective energy the reaction time increases. In the thought-disordered schizophrenic, this critical period lasts between 4 and 6 msec. In other words, the schizophrenic is sensitive to changes in stimulation which the normal subject cannot perceive, even though various methods for eliciting earlier detection in the normal have been tried. In still a third experiment we, as well as others, found that the average evoked potentials to light and sound showed the smallest amplitude for schizophrenics, highest for normals, with the depressives in between. The expected greater variability for schizophrenics also appeared.

The evoked potential in schizophrenics is not only smaller but it is very different in shape from the depressive’s and normal’s evoked potential. These differences in shape were so hard to specify quantitatively that we resorted to clinical methods. For each of a large number of subjects, most of whom had never seen an evoked potential waveform before, we asked which of three waveforms was most different—without specifying any criteria. The waveforms included one from a schizophrenic, one from a depressive, and one from a normal subject. For each of our subjects in this clinical study, we used a different triplet of waveforms. Schizophrenic waveforms were chosen as most different in 60% of our choices—almost twice as often as they would have
been selected by chance. Depressive records were chosen as being odd 30% of the time, approximately what you would expect by chance, and normal records were rarely selected as odd—only 10% of the time.

The effect of uncertainty regarding a forthcoming stimulus was far greater—three times as great for normals than for the patient group. This is in contrast with the effect on reaction time in which uncertainty affected the patients more than the normals. Thus, psychomotor responses seem to be affected differently than perceptual responses when uncertainty is introduced in the performance of schizophrenics and normals. Normals and depressives show higher amplitudes when a modality switch occurs, while schizophrenics show the higher amplitude when the same stimulus follows in succession.\textsuperscript{13}

To discover the full import of each of the six etiological models for mental disorder, we have to resort to a strategy which will permit the assessment of each of them separately. This presents us with a dilemma, since none of these models are sufficient in themselves. They are often necessary, but not sufficient alone in eliciting a given disorder. One strategy which has developed recently is to determine for each model, the particular parametric values of their variates which are likely to produce a high risk for the emergence of a given illness. Thus, for the genetic model, it is generally agreed that a member of an identical pair of twins, whose co-twin has already developed schizophrenia, has a rather high risk of developing schizophrenia himself. Similarly, for the ecological model, an individual raised in a deprived, very poor environment is generally regarded as having a high risk of developing schizophrenia. By selecting individuals who are identical co-twins of schizophrenics, or offspring of schizophrenic parents, we can determine the importance of such factors in the development of schizophrenia, especially if the parameters of the other models are permitted to vary randomly. Similarly, if we select individuals who have undergone the stress and strain of growing up in an ecological niche full of deprivation, poverty, and other specific disadvantages, we can determine the relative importance of these various parameters in producing or eliciting schizophrenia. Again, if we want to determine the strength of the interaction between genetics and ecology in the elicitation of schizophrenia, we can take individuals who stand in the high-risk category in both of these variables. Two sophisticated examples of these interactions are the studies of adoptees by Rosenthal and Kety\textsuperscript{18} and the proposed studies of socioeconomic stress by the Dohehnwends.\textsuperscript{4}

The tendency to deal with ecological factors as the sociologist used to do without paying attention to the characteristics of the individual on whom the ecological forces were impinging has given rise to the so-called ecological fallacy. Here, the covariance between two variates such as rate of schizophrenia and average rental in each area of a large city, was interpreted as representing the relationship between these two variates and was usually found to be negative. However, this covariance dealt only with the mean values for the areas—the rate for the area and the average rental for the area. The total covariance includes also the covariance within the area—within the individuals living in each area, and the total relationship between rental and rate must include this source of relationship also. That is why the covariance between the averages is regarded as reflecting the ecological fallacy. Similarly, the clinician usually deals only with the within-group covariance of his patients, forgetting about the between-group covariance. This is the clinical fallacy. Both sources of covariance must be dealt with if we are to understand the total picture.
The great obstacle in this approach is the absence of good taxonomies for the parameters of the various models that have been proposed. One striking example is the relation between intelligence and heredity as Jarvik and Erlenmeyer-Kimling\textsuperscript{10} have shown. If we take pairs of individuals who vary in their degree of blood relationship from pairs selected at random to pairs of grandchildren, cousins, parent-child, siblings, dizygotic twins, and monozygotic twins, it is well known that the correlation for groups of such pairs rises with rise in blood relationship from zero to 0.90+. Similar attempts to correlate pairs varying in the degree to which their ecological niches are similar result in no such systematic relationships. Why? Probably we have not yet found as good measures of similarity of environment, as we have already found for similarity of genetic endowment.

Once we have pushed the main effects of our models as far as we can, we will have to resort to discovering their interaction effects. Here we are faced with the fact that our methodology has far outstripped our data collection. We already have several powerful methods for analyzing such data when they become available. The factor analytic method which would reduce the host of parameters for each model into a single or only a few underlying components is probably the best known. It makes certain assumptions about the data which are not always justified, but it does a good job of bringing the analysis into a comprehensible scope. A second approach is that of the discriminant function, which can be applied to determining whether the data differentiate between such contrasted groups as patients and normals or between subgroups of patients. To find the subgroups, certain typologic analyses have become available which help determine whether types exist and if so, the best way to classify a group into subtypes. A third approach, most suitable for dealing with our varieties of models, is the canonical correlation approach. This approach attempts to discover the relationship between groups of variates belonging to one universe—say the ecological—with a group of variates belonging to another universe—say the genetic.

In our case, by utilizing ecology and genetics as examples, we could find the canonical correlations between the ecological, genetic, and behavioral variables in the form of dimensions of psychopathology, and then determine the contributions of each variate to the degree of psychopathology produced. This could be extended to include all six models together with the psychopathologic behavioral measures. The patterns of correlational structures in two contrasted groups of normal and deviant individuals would then serve as a basis for differentiating them as well as for classification purposes.

The most fruitful studies now in process are those which involve the intersection between two or more models. In fact, the very name neuropsychopharmacology is a testimony to the fact that it is in the intersection between neurophysiology, psychology, and pharmacology that the pay dirt lies. Perhaps the best known interaction is that between the ecological and genetic models or, as it used to be known, the interaction between nature and nurture. Another well-known interaction is that between the learning, the internal environment, and the neurophysiologic models which is best represented by the concept of psychodynamics and somatopsychics.

The interaction between the internal environment and neurophysiologic models is exemplified in the assumption that the modulation of neural transmitters by foreign substances (drugs) or by excess of endogeneous substances within the internal milieu is what lies at the bottom of the disturbances in processing information in schizophrenia or development of mood disturbance in affective disorders.
CONCLUSION

Neuropsychopharmacology is essentially a biologically oriented discipline which assumes, following Dubos, that “all the constituents and processes found in living things, including man, obey the laws of inanimate matter.” In describing the proceedings of a recent international congress on “From Theoretical Physics to Life,” Dubos indicates that though general agreement was reached on the above statement, the moment the discussion shifted to the bearing of scientific knowledge on human behavior and on social action, pandemonium reigned.

“We know a great deal concerning the physiochemical phenomena that make life possible, and we can formulate reasonable hypotheses concerning their origin and evolution. We can imagine, even though we do not completely understand, how each particular living thing is shaped by genetic constitution, experiences and environment... the physiochemical forces provide (however) only the props and stage machinery.”

Thus far we have described the etiologic models as blind forces which control man's destiny and to some extent, given the current scene, this is a true picture. For the ecological niche in which man finds himself does determine his well-being, his genetic make-up does limit his potential, his developmental past and learned behavior do confine his future, his internal environment and neurophysiologic make-up control his behavior. 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 omitted perhaps the most important determinant of man's stage behavior—his ability to be a self-starter, to alter developmental trends, to modify the internal environment as well as his neurophysiologic 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. It need not take eons to accomplish, for we can produce changes for the better even in our own lives and within our own lifetime. The options that such changes make possible are the real problem we are facing. How are we to decide what changes to bring about, and where does the moral and ethical imperative come into play? I am afraid that such questions are beyond my ken, and perhaps beyond the ken of science. Nevertheless, they are issues which we can not help but face, and only by increasing our scope to include within our ranks philosophers of science and ethical and moral scholars, can we hope to come to any agreement on these issues.

SUMMARY

To summarize briefly, there are many models for psychopathology some of which we have sketched, while others were omitted. In choosing between these models we must remember that the choice is not between good and bad models, but between the testable and the untestable. Furthermore, it is not sufficient to provide models for explaining the underpinnings of behavior. Even though we are far from having attained this goal, as we make progress, we must extend our domain to include the moral and the ethical problems which our discoveries raise and it is not too early to raise these issues now. Otherwise we may parallel the impasse which physics had to face after the invention of the atomic bomb.
REFERENCES


