Suiting Therapeutic Intervention To The Scientific Models of Etiology

by

Joseph Zubin

To be delivered at the Second International Schizophrenia Symposium
"The Role of Mediating Processes in Understanding and Treating Schizophrenia"

Bern, Switzerland
September 10th - 12th, 1987


Supported by the Medical Research Service of the Veterans Administration.
Suiting Therapeutic Intervention to the Scientific Models of Etiology

Since descriptive psychiatry offers only the surface exploration of psychopathology we must turn to etiology for the deeper understanding of our problems. It has become quite clear during the last several decades that the factors in the etiology of schizophrenia are less well established than the factors in the efficacy of therapeutic intervention. The former are still highly theoretical in the form of scientific models whose tenability is often difficult to establish while the latter can be tested more objectively through clinical trials. In this manner, the efficacy of neuroleptic therapy and of the various behavioral and psychosocial therapeutic interventions has been examined and some found to be wanting (e.g. renal dialysis). Nevertheless, the therapeutic clinical trials probably arose as a result of some etiological considerations and for new therapeutic approaches we need to turn again to our etiological models. However, the connection between etiological models and therapeutic intervention has never been examined. As a result we have elaborate etiology on the one hand and specific therapies on the other but the two domains pass each other by. The purpose of
this paper is to weave the threads of practice into the web of theory.

There is, of course, the possibility that treatment is independent of etiology and that biological etiology can be dealt with successfully by psychosocial intervention and vice versa. I believe, however, that this may be the result of our ignorance of the link between etiology and intervention rather than of its absence.

Beginning with the vulnerability model which can serve as a superordinate model for all the etiological models, we shall try to indicate what its specific underpinnings are, and what therapeutic intervention is called for. We will do the same for each of the submodels (ecological developmental, learning - habit formation, genetic, internal environment, psychophysiological and neuroanatomical models).

A summary of examples for testing the efficacy of each of the therapeutic interventions for each model will be attempted.

It will become apparent in the course of this that the etiological models are far from independent of each other and their needed integration has already been stressed by Ciompi and others at our last meeting. Nevertheless, we shall treat the problem of harnessing each model to its therapy as if we were dealing with a problem of analysis of variance and push the main
effects as far as possible before appealing to interactions.

One of the underlying themes that will emerge is the contrast between the Hippocratic trend toward natural healing of the patient and the more aggressive trend for treating the disease. Ackerknecht (1973) points out the see-saw between these two trends in the history of medical treatment. When natural healing was dominant the aggressive biological and behavioral approaches were neglected, yet when the pendulum swung back in the other direction, natural healing approaches declined. Now, the more aggressive approach is dominant and consequently the forces of natural healing are held in abeyance. It is to the credit of the organizers of this symposium that we are given the opportunity to swim against the current and enlist the natural healing capabilities of the patients in our discussion.

Another theme that will emerge is the contrast between the qualitative and the quantitative methods in psychopathology. In its present state of development psychopathology resembles more fields like linguistics than physics. It must be remembered however, that even the physical sciences with their highly objective quantitative methods had their beginnings in the subjective intuitive qualitative approach. Long before we had thermometers, subjective warmth was probably the
concern of our primitive forebears. The ancient Egyptians developed a rating scale which ranged from the hottest day of summer to the coldest day of winter in 4 steps. The final step in the development of the measurement of subjective warmth came when it was observed that mercury and other substances expanded as subjective warmth increased. That is how the thermometer was born with its zero point fixed at the temperature of the coldest day of winter which Farenheit experienced in Greenland. (Zubin, 1965)

Mayr (1982, p.54) has pointed out that "The champions of quantification tend to consider the recognition of quality as something unscientific or at best as something purely descriptive and classificatory... Quantification is important.... but not to the exclusion of all qualitative aspects. These are particularly important in relational phenomena, which are precisely the phenomena that dominate living nature. Species, classification, ecosystems, communicatory behavior, regulation, and just about every other biological process deals with relational properties. These can be expressed, in most cases only qualitatively not quantitatively."

The earliest clash between the qualitative and the quantitative approaches can be traced back to the early Greeks and the ancient Babylonians before the days of Alexander the Great. Derek de Sola Price (1975)
points out that the ancient Babylonians were masters of quantification and measurement but poor on qualitative conceptualization. Meanwhile the ancient Greeks excelled in geometry and other qualitative relational approaches but were poor on measurement. It wasn't until Alexander the Great brought these two ancient civilizations together that Greek conceptualizations and Babylonian measurements were combined into modern scientific strategies in which quantification and measurement probed the tenability of conceptualizations.

Psychopathology prior to the 1930's was primarily a qualitative science untrammelled by quantification. Such quantification as did exist dealt primarily with rates of incidence and prevalence, release rates, mortality, etc. Though these are important they had little if any connection with the mainstream of conceptualization in the search for etiology and treatment. As the impact of interdisciplinary approaches began to be felt, with the entrance of other sciences such as biochemistry, genetics and psychology, a movement in the direction of quantification began. An example is the interaction (perhaps apocryphal) between Hudson Hoagland and William Malamud at the Worcester State Hospital in the early decades of this century. Hoagland found some biochemical change in Malamud's patients and asked to see Malamud's data on
the same patients. Malamud handed him his voluminous case histories. "Are there no numbers here on their behavior?" Hoagland inquired. Malamud answered, "No, but if you want numbers I'll make them up for you." That night with the help of Sands he converted his descriptions of behavior into rating scales.

The biometric approach which was developed at Worcester was spearheaded by Jellinek and followed up by our own Biometrics Research Unit at the New York State Department of Mental Hygiene and the Biometrics Branch of the NIMH headed by Mortimer Kramer as well as by the quantitative contributions of the Institute of Psychiatry of the Maudsley Hospital (Lewis, Wing, Eysenck, et al.). Rating Scales, systematic interviews, dosage problems, and electrophysiological measures all contributed to a surge in the direction of quantification expressing itself in more and more sophisticated statistical analyses: regression equations, survival curves, discriminant functions, path analyses, factor analyses, etc. Qualitative studies continued in psychoanalysis and outcome studies; e.g., Franz Alexander's 'escape into process' (Zubin, 1962) when he gave up trying to demonstrate the efficacy of psychoanalytic treatment. Eventually the qualitative approaches came into definite decline. I should be the last to complain about the trend for quantification, but I believe it has gone too far! I
The vulnerability model postulates that the persistent characteristic of schizophrenia is not the enduring schizophrenic episode itself, but the vulnerability to the development of such episodes of the disorder. The episodes themselves are time limited "states" of longer or shorter duration, but vulnerability itself is a persistent trait. However, vulnerability may remain latent until it is triggered into expression by some stressor. Strictly speaking, the vulnerability model is not in itself an etiological model - it relegates specific etiology to its submodels. In considering the vulnerability model, we must also consider the effect of certain moderating variables such as the premorbid personality, the social network and the ecological niche which the person occupies. These, if favorable, will abort the episode even in a person who is highly vulnerable and who undergoes a triggering stressor. If they are noxious, however, they will elicit and exacerbate the episode. The episode, once developed, does not persist a lifetime, but finally disappears and permits the patient to return more or less to the initial premorbid status. If the premorbid status was good, we tend to regard the patient as improved or recovered. But if the premorbid status was poor we tend to regard the patient as unimproved or worsened even though the episode may have ended and the patient returned to the
premorbid status. Some of the apparent chronicity in schizophrenia may be explained on this basis with many of the so-called chronics being in reality only pseudo-chronics, whose episodes have ended.

What can be done to prevent the development of the initial episode or of repeated episodes and what therapeutic strategies can be employed to attain these ends?

How can we suit therapeutic strategies to the vulnerability model?

As for preventing the initial episode, we must identify the individuals who are vulnerable by discovering identifying markers, a technique which is developing rapidly at this time and which is described in several recent publications (e.g., Zubin, Steinhauer, Day, and van Kammen, 1985). Once the high risk individual is identified, a survey of his coping methods under stress has to be undertaken and an educational regime developed for improving his coping skills, if necessary. The ethical problems involved in the detection and identification of vulnerable individuals as well as in the initiation of educational prophylaxis are still unsolved problems, but these are the directions in which our efforts might be devoted. Similar paths for the prophylaxis of diabetes, high blood pressure, heart disease, and other disorders have already been evolved and these can serve as prototypes.
As our knowledge of the immune system for monitoring stress develops, perhaps it can replace the current techniques of interviewing for life-event stressors. These strategies may be especially helpful in dealing with relapse. For prevention of relapse we need to know, first, whether the current episode is still in effect or whether it has run its course. For this, we have such tests as the apomorphine challenge or the ritalin challenge (Zubin et al., 1985). Once it is determined that the episode is ended, a monitoring of the patient's level of stress through some suitable gauging device such as the interview for life events or measures of the immune system's response to stress can be initiated. The educational strategies described in the prevention of the initial episode can also be used in relapse prevention. However, we have an additional source of information in the form of the strategies which the recovered patient himself resorts to when threatened with relapse -- the self-monitoring that is often reported anecdotally at the present time, by recovered patients. These should now be recorded by the therapist in a systematic fashion as a guide for future prevention.

Let us now turn to the submodels of etiology.

Time does not permit to give in detail the relation between each of the etiological models and the optimum treatment for schizophrenia. It is my hope
that the contributions of this symposium will provide such detail. I will, however, present a brief assessment of the seven extant models but expand on the most successfully applied model - the internal environment model.

2. The ecological model and the developmental model

It should be pointed out that up until recently I tended to regard the ecological model and the developmental model on the same level as the other etiological models (learning, genetic, internal environment, neurophysiological and anatomical). However, I found it difficult to find the specific areas of behavior and brain functions belonging to the ecological and developmental models until I realized that the ecological model was in reality a spatial model and the developmental model a temporal model. The "where" and the "when" of the behavior and brain function related to the behavior, are the domains of ecology and of development, respectively, but the actual behavior itself is related to the other etiological models. Ecology and development, however, do have special characteristics of their own.

For example, despite the controversy that exists regarding the concept of "critical periods," there are certain periods in development which appear to be critical in the development of psychopathology and which are truly indigenous to development. The two
most interesting periods in this regard are: First, the migration of the neural cells from their development in the ventricular area to their superficial cortical layer (Rakic, 1972; Goldman-Rakic, 1987). This occurs early in the fetal stage in primates about the time when the perinatal and postnatal deviations develop. Ultimately some of the migrant neurons lose their way and do not reach their goal. And second, the sloughing off of the supernumerary neural cells at adolescence (Feinberg, 1982) might explain why first episodes of schizophrenia tend to occur at adolescence. The gender differences in the age of emergence of the first episode and the generally better outcome for females are other examples from the developmental model.

The ecological model, strictly speaking, represents only the external physical - social - cultural forces impinging on the ecological niche which the person occupies in life. Hutchinson (1978) has provided a scientific definition of the ecological niche in the following term quoted from Gould (1987). He contrasted the earlier definition of ecological niches as merely geographical addresses of the organism or as the result of the range of activities (feeding, nesting, etc.) performed by the species. He concluded that the interaction between these two aspects constituted the niche. "Organisms ..... create ecospace (niches) through their activities but the
nature of physical space and resources sets important limits."

We shall follow this definition in our discussion and apply it to the human species.

This model is in contrast with the other etiological models which deal primarily with internal forces. The spatial aspects of the ecological model inhere in the role of such factors as density of the microniche the person occupies and its relation to the population density of the macroniche or milieu in which it is imbedded (Zubin, Magaziner, and Steinhauer, 1983) involving factors like socioeconomic status, marginality, majority-minority status, etc. Up until now, the evidence for these spatially and time referred forces serving as etiological sources has not been established as solidly as the role of the forces associated with the other models. It may indeed be the case that they are rarely or never causal in nature, but serve to elicit or moderate other causal factors emanating from the other models, such as the genetic or internal environment models.

Similarly, in trying to describe the developmental model I found that unlike the genetic or other models, there existed no substantive contents for the developmental model except the longitudinal aspects it implied. The developmental model represents the outcome of all etiological forces in time. There was
no specific domain for development itself except in the change brought about in time from the other models and their interactions. The developmental framework dealt with age related events and thus represented a superordinate model. A good example of the developmental model in operation is provided by Weinberger (1986). The essential points of his model are that some lesion (in the limbic lobe or frontal lobe) develops early in life. It is not the lesion alone, but the effect of this lesion on brain maturation that brings about the disorder (neither the location nor cause of this lesion are as important as its influence on maturation). Thus, according to this model, the primary etiological agent is the lesion, yet its effects in time on maturation are the proximate cause of developmental anomalies associated with schizophrenia.

That time and space dimensions are important factors in behavior, both normal and abnormal, hardly needs to be demonstrated. However, neither of these two important dimensions, so crucial in the physical sciences, play an important part in the theories and models proposed thus far for psychopathology. When we speak of time, we mean the when or longitudinal aspects of behavior and when we speak of ecological niche, the where aspects. As far as time is concerned, two considerations are important - the time or period when
the behavior occurs and the time when its etiology began. As far as the ecological niche is concerned, the demographic, social-cultural-physical characteristics of the niche currently occupied as well as those of the previous niches are important influences on behavior.

Our chief concern is the psychopathology of schizophrenia. Accordingly in discussing the time dimension of our proposed model, we shall delineate the beginnings of the course of the illness, its longitudinal course in the premorbid or preepisode period, during the episode and post-episode course. As far as the ecological niche is concerned we shall indicate the characteristics of the major niches occupied by the person premorbidly, at the point of development of the episode as well as during post-episode.

How to deal with the various deviations arising in time (developmental) and those arising due to space (characteristics of the niche) is described in a vast literature. Thus, the increase in rate of schizophrenia in offspring of mothers who lose their husbands during pregnancy (Huttunen, 1978), the higher risk for adolescents who never experience intimacy in their friendships (Kreisman, 1970) and the higher risk of schizophrenia for perinatal injuries seem to require
special interventions to counteract their malignant effects.

3. **Learning Theory Model**

   The neo-learning theory model assumes that though there may be neurophysiological underpinnings of the deviant behavior in psychopathology, the overt behavior itself can be targeted for elimination by learning theory strategies.

   Under the learning theory model consider an obsessive-compulsive disorder which had a strong operant component. This operant component may be amenable to the application of operant principles such as rearrangement of contingencies so that reinforcement of non-compulsive behavior would become a prominent feature. On the other hand, if the disorder is respondent in nature, the application of respondent principles would be applied. Appropriate interventions would include desensitization or response prevention (Levine & Sandeen, 1985).

   It is often necessary to utilize the principles of a given model even when it is not the primary cause of the disorder. The principles often provide a necessary preliminary step in treatment. For example, even when the learning theory model (cognitive) seems to be the most suitable explanation of the etiology, such as is the case when a critically ill wife is the source of the anxiety, the internal environment model with its
Our greatest therapeutic advances have occurred in the internal environment model where the discovery of neuroleptics has practically revolutionized treatment. However, despite its advances, it has not brought us any nearer to the etiology of schizophrenia. It has, however, opened our eyes to the workings of the normal brain and its neurotransmitters. Furthermore, after 30 years of investigation it still presents us with a tremendous challenge. Why is it that despite the impact that the neuroleptics have had on the acute phase, they cannot prevent relapse nor new episodes in patients even when compliance is assured by intramuscular depot preparations? What mechanisms are at work counteracting the efficacy of the drug? Does some habituation develop which makes the drug lose its efficacy? Does the ability of the drug to contain the stress produced by the disorder weaken? Does the neuroleptic treatment interact with other transmitters such as nor-epinephrine to elicit a relapse? Or do the relapsers have a more severe form of the disorder? From the point of view of vulnerability theory, the relapse or even the development of a new episode in a recovered patient could be attributed to an increase in stress probably initiated by either external or internal stressors which is beyond the tolerance provided by the neuroleptics. If this is the case, continual monitoring of stress levels perhaps through
the surveillance of the immune system may provide an indicator for intervention. It is in this connection that psychosocial factors can play a very important role by invoking nature's healing tendencies. These can be brought about by cognitive and behavioral strategies for maintaining and aiding and abetting the morale of the patient in his search for self liberation from his affliction.* Eliciting his inner tendencies towards self healing by suitable rehabilitation methods may be the most important aid in the prevention of relapse and the maintenance of his normality when drug therapy fails. Only by returning to the Hippocratic belief that the patient rather than the disease should be targeted by therapy, can we abort new episodes. This is the challenge that psychosocial variables have to meet, and it is most fortunate that this conference provides a platform for such considerations.

SUMMARY

There appear to be three central themes: (1) the contrast between quantitative knowledge and qualitative, (2) the fact that biological factors may be wired in but psychosocial are not, and (3) that we have not come very far in matching treatment to etiological theories.

* Naturally, the search for other drugs may provide better protection against relapse for some patients (e.g. clozapine)
Psychotherapy is really the treatment side of the psychosocial model for etiology (ecological, developmental and learning). We should not overlook the fact that a good therapist is really a teacher who opens up new options which the patient was not previously aware of, and which aid the patient in finding his own coping strategies that will provide "natural healing". The poorer therapist may, perhaps, lean too heavily on the phenothiazines alone believing that something must be "done to" the patient who is nothing more than a mass of wired in circuits and chemicals, rather than enlisting his or her help to try new strategies for coping.

This could all be related back to our plea that we not overlook the qualitative side of things. Perhaps, we will one day quantify the interactional aspects of patients and therapist so that we know why the same therapy, e.g., cognitive behavioral, works with one therapist and not another. Of course, too often we assume that it is poor matching between the type of therapy used and the particular patient, when, in fact, it may be a poor match between therapist and patient. Again, another example of those intangible qualitative factors that are so important.
Joseph Zubin, Ph.D.
Veterans Administration Medical Center Highland Drive
and
Department of Psychiatry
University of Pittsburgh School of Medicine
REFERENCES


Rakic, P. (1972) Mode of cell migration to the superficial layers of fetal monkey neocortex. The Journal of Comparative Neurology, 145, 61-84.


