A Developmental Model for the Etiology of Schizophrenia

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I. Introduction

It's a great honor to be invited to participate in the Symposium in memory of Lauretta Bender. I had known Lauretta ever since her beginning Bellevue days and often participated with her in the meetings of the American Psychopathological Association in which she was very active and served as its president in 1962. In addition, I had been teaching a course at Columbia University's Department of Psychology in Projective and Cognate Techniques, and the Bender-Gestalt Test was one of the instruments we dealt with. The manual for this course even
contained an objective scoring scheme and a modification of the
instrument which I prepared for my class.

Lauretta had a charismatic personality as evidence by the
number of promising young people who were enthralled by her
teaching and research. Among them are now counted some of the
leaders of our field: Al Freedman, Chairman of the Department
of Psychiatry of the New York Medical College, and former
president of the APA and ACNP Robert L. Spitzer, Director of the
Biometrics Research Unit at the New York State Psychiatric
Institute, my successor in that post, and many other outstanding
clinicians and researchers, and a host of social workers who
hung on her words which included my wife who was then a budding
social worker.

II. The Etiology of Schizophrenia from the Developmental Point
of View

It is by now a well recognized truism that we are abysmally
ignorant of the etiology of schizophrenia though we have made
some progress in describing it and diagnosing it and even
treating it. To compensate for our ignorance of etiology we
have proposed seven scientific models of supposed etiology and a
superordinate model for integrating them into a vulnerability
paradigm. These models have been dealt with elsewhere (Zubin
1972). Here we shall deal primarily with the developmental
model.

Historically, the developmental approach has given rise to
such hypotheses as (1) the schizophrenogenic mother, (2) the
effect of interaction between mother and infant, (3) the role of the family structure, (4) pseudomutuality, (5) double bind, (6) communication deviance and several others. Today, we shall leave these hypothesis to history but deal only with the current scene.

This lecture consists essentially of two parts: a theoretical discussion of the developmental model and (2) the evidence for the tenability of the model. The theoretical portion is largely mine while the empirical portion is largely the work of Drs. Richard Feldman and Suzanne Salzinger.

II. The Scientific Models of Etiology

1. (Give a description of each of the models and indicate that we will pay special attention to the developmental - ecological model)

2. The developmental model.

Up until recently I tended to regard 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 developmental model until I realized that the developmental model was in reality a temporal model, dealing with the "when" and not the "what" of the behavior and brain function related to the behavior. The actual "what" of behavior itself is dealt with in the other etiological models. Development, however, does have special characteristics of its own.
For example, despite the controversy that exists regarding the concept of "critical periods," there are certain stages which appear to be critical in the development of psychopathology and which are truly indigenous to development. The two most interesting phases in this regard are (1) the migration of the neural cells from their development in the ventricular area to their superficial cortical layer (Rakic, 1972; Goldman-Rakic, 1987 and Geschwind). This occurs early in the fetal stage in primates about the time when the paranatal and postnatal deviations develop and probably also occurrs in humans. Ultimately some of the migrant neurons lose their way and do not reach their goal; (2) 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. It is likely that reinforcing eye contact as well as body contact have critical periods for which proper parenting is a necessity, which also holds true of early linguistic behavior.

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 arranged in time. There is no specific domain for development itself except in the change
brought about in time in the other models and their interactions.

That the time dimension is an important factor in behavior, both normal, and abnormal, hardly needs to be demonstrated. However, time, so crucial in the physical sciences, plays an unimportant part in the theories and models proposed thus far for psychopathology. 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. We will discuss each of these factors separately.

Our chief concern at this symposium 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.

How to deal with the various deviations arising in time (developmental) 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) and the higher risk of schizophrenia for paranatal injuries seem to require special interventions to counteract their malignant effects.

What are the requirements of a developmental model of schizophrenia? We suggest 3 components: (1) evidence of early preschizophrenic or possibly even prenatal deviance at some
level which could range all the way from internal biological processes to social behavior, (2) increasing deviance with age, into the period of greatest risk for schizophrenia or until an actual episode develops; and (3) specificity of signs or markers so that even if not everyone who has them becomes schizophrenic -- the individual who have them are more likely to develop schizophrenia than some other condition. The markers could help to identify them so that preventive strategies could be initiated. These components seem to us reasonable, if not absolutely essential. Deviance, in principle, need not appear early, since "development" is, after all, a life-long process and is not to be taken to be synonymous with "child development"; and, in principle, onset could be sudden and not preceded by a period of increasing deviance and could occur at any point in the time span, including old age. There could even be multiple "schizophrenias," some fitting a developmental model better than others. Evidence for genetic loading plus the existence of children who appear to meet all or most of the criteria for actual schizophrenia (e.g., Cantor et al., 1982) support the search for early expression of deviance, and empirical behavioral data from high risk studies support the claims for both early expression and, to a lesser extent, predictive specificity of deviance, although much of this work can only be considered preliminary. Therefore, we feel that the three components we have stated are, at least for now, the most heuristic.
In its most basic form, the model is of course transactive, recognizing that any early insult or predisposition -- whatever its nature (genetic, neurophysiological, behavioral, etc.) and however arrived at (inherited or acquired) -- exists in a changing organism developing in a changing environment. This provides a general mechanism or context for either the amelioration or exacerbation of deviant biological and behavioral phenomena which at their initial stages might not in themselves be noticeable nor remarkable.

As to the exact nature of the initial insult or predisposition, the most likely candidates would appear to be genetic, biochemical, and neurologial. The genetic (familial) evidence is well-known; it is the foundation of high-risk research designs and it is a principal argument against a developmental model based entirely on external environmental factors (which, however, might still be critical to the behavioral expression of the condition).

As for neurology, Weinberger's (1987) model, speculative as it is at this stage, is a true developmental model in that neither the cause not the location of the postulated early brain lesion is as important as the influence of that lesion on brain maturation. Thus, according to this model, the primary etiological agent is the lesion, yet its effects on maturation of the brain areas related to symptom development are the proximate cause of the anomalies associated with schizophrenia. The presumed presence of the originally "silent" lesion postulated by Weinberger will no doubt lead to attempts to
demonstrate its presence. Such searches go under the general category of the search for "markers" which identify the individuals at high risk. The deviation indicated by the marker may not reach behavioral expression immediately or may even never do so. If we ever detect the DNA segment containing the allele or alleles for schizophrenia, this would be another silent marker of high risk even though it may never express itself. One marker of this type has been reported by Venables (1978) in the area of attention. As is well known there are two types of attention: involuntary and voluntary. An example of involuntary attention is the orienting response to threatening external stimuli. This response must have been wired in during evolutionary times and those who did not develop it failed to survive. Voluntary selective attention, according to Luria following Vigotsky's model, is not an inborn reflex, but requires mothering and social experience before it develops i.e. it is a psychosocial response and according to Vigotsky has no biological roots at all. Whether this is so or not is debatable, since every bit of behavior is biologically based, but perhaps Vigotsky's intention is to indicate that without social elicitation, selective attention would not develop. At all events it is likely that in contrast with the involuntary orienting reflex which is wired into the brain, the orienting selective attention belongs to the neuroplastic part of the brain where the pathways are still undiscovered or they may be so idiosyncratic that they do not have a common pathway. This may be the reason why hard headed scientists prefer the
biological indicators to the psychosocial indicators for schizophrenia.

One type of orienting response is obtained when an innocuous stimulus is presented under conditions when no specific task is imposed, so that habituation will eventually set in when the task is repeated. One of the most popular indicators used to monitor this response is the electrophysiological measure of skin conductance.

Venables et al (1978) applied this technique to an unselected group of infants and children in Mauritius. Some individuals do not show any changes in their skin conductance under these conditions. They are called the non-responders. Venables et al identified a group of non-responders in 3 year old children and these were followed up to 6 1/2 years of age. Already at that young age they displayed more social isolation and less constructive play than did their responding peers. This relationship between orienting responding and social emotional withdrawal can not be blamed on hospitalization, medication or labelling though whether it is a product of lack of proper parental or experiential reinforcement remains an issue. (Bernstein) Regardles of this problem, the orienting response does provide a high risk indicator which may eventually prove to be a marker of vulnerability identifying at least a portion of the vulnerable population.

Numerous other studies find evidence of early deviance, sometimes as early as infancy. Barbara Fish's longitudinal study and the Jerusalem Infant Development Study (Marcus et al.) are
among those showing evidence of basic dysfunction in high-risk children in infancy, while Massie and Rosenthal's analysis of early home movies of children diagnosed subsequently as psychotic shows sensorimotor deviance in the first two years of life.

The Stony Brook and the New York high risk studies are both finding a variety of deviance in early and middle childhood.

The Stony Brook project has reported evidence of childhood deviance on a variety of speech measures (Harvey et al., 1982); on cognitive-attentional measures (Winters et al., 1981), although children of unipolars sometimes perform as poorly as children of schizophrenics; and on peer ratings of competence (Weintraub et al., 1978), although again some comparisons show little difference between children of schizophrenics and children of depressives, with one important exception to be specified shortly. The New York project also finds poor performance on attentional tasks for the high-risk children, and less deviance for the psychiatric controls than the Stony Brook project reports. Cornblatt and Erlenmeyer-Kimling (1985) attribute this difference between studies to what they say is a more "liberal" criterion for deviance and the tapping of more complex cognitive functioning, not as likely to show deficits specific to any one kind of psychopathology, in the Stony Brook work. In any case, these and other high-risk studies (e.g., Fish and the Israeli studies) report deviance on a variety of measures for the offspring of schizophrenic parents.
Furthermore, the New York project and others are finding that the high-risk children showing early deviance become increasingly dysfunctional, or show behavioral deviance in multiple ways, as they get older -- as we suggest should be expected from a developmental perspective.

As to specificity, the evidence at this stage must come almost exclusively from differences between preschizophrenic high-risk children and comparison groups, since few cases in any of the longitudinal studies have actually developed schizophrenia or even entered the period of greatest risk. Some of the most interesting evidence with regard to specificity comes from the New York project. Not only are more high-risk children than psychiatric or normal controls deviant on the attentional measures, but the attentionally deviant high-risk children become increasingly deviant in social and other behavior as they get older, while children in the other groups do not. Thus Erlenmeyer-Kimling and her colleagues believe that they may well be tapping a specific predictor for schizophrenia or closely related disorders. An interesting finding in the Stony Brook studies was that the older (children in Grades 6 - 9) daughters of schizophrenic mothers were different from the daughters of depressed mothers on the ratings given by their classroom peers. Weintraub et al. commented at the time that this finding was "the first clear differentiation, in the realm of competence, of the offspring of schizophrenics from the offspring of a psychiatric control group (1978, p. 417). The differential response by peers to high-risk children, if it
holds up as a widespread phenomenon, would not only bolster the
social validity of behavioral differences detected by other
measures, but would have enormous developmental implications
because of the significance of peer relationships for child
development generally.

As we have said, a developmental model is essentially
transactive, one in which a maturing organism interacts with a
changing environment resulting in recursive effects which modify
both the characteristics of the organism and the nature of the
environment. In normal development, this means that both the
organism and the environment, particularly the social
environment, are engaged in mutual adaptation to each other's
requirements through assimilation and accommodation (Piaget),
resulting in growth and normal functioning appropriate for
increasing age. In a child who gives evidence of early
behavioral dysfunction, let's say as a result of a genetic
predisposition for schizophrenia, the behavior can produce
aggravated responses in the social environment, that is, in the
caregivers, which in turn affect in feedback fashion the already
vulnerable child in such a way as to exacerbate the
dysfunctional behavior. One could envision that the result of
such a recurring sequence would produce increasing dysfunctional
behavior not only in the child but in the parents as well. We
have already presented some of the evidence for such increasing
deviance in the child. Thus we need to understand the
developmental progression of the child, the mediating effect of
the dysfunction and the environment, both social and physical, and both internal and external.

For everyone throughout the course of development, there are life-stage transitions, developmental milestones to be met, that are of major significance. One can imagine that due to increased stress associated with these periods of transition, people become more unstable or more susceptible. These periods may be considered to be somewhat analogous to the old concept of critical periods, which has been part of the developmental literature for a long time. We think, however, that the value of considering such periods particularly important stems more from the fact that they single out points in time for scrutiny and study rather than from the fact that they are always more important than any other time period during the course of development. With respect to the onset of schizophrenia, however, we would want to look at the transition between the pre and neonatal periods as well as the perinatal period where neurological processes are in a period of rapid growth and proliferation and differentiation (Rakic studies) (Weinberger) as good points to perhaps find some early insult or markers for the condition. Adolescence, particularly late adolescence, is, of course, the period where people are most at risk for actual onset of schizophrenia. The work of Feinberg (1982/83) suggesting the possibility of a reduction in cortical synaptic density in adolescence, is particularly suggestive.

The evidence for the probability of an early biological insult was cited earlier both in the high-risk studies and in
the early detection of deviance in young psychotic children. We mention it again here merely to point out that such early behavioral deviance as, for example, in sensorimotor functioning, certainly puts the child at a disadvantage in coping with the stresses engendered both by the biological changes (internal environment) the child must adapt to, and by the major external environmental changes that occur during and between childhood, adolescence, and early adulthood.

Let us come to a consideration of the environmental variables. In order to develop normally, infants must be able to establish mutually reinforcing patterns of interaction with their parents. There is increasing evidence that the mothers of psychotic babies and high-risk children behave differently from other mothers, providing a poorer environment, i.e., less play stimulation, fewer learning experiences, and less emotional and verbal involvement (Goodman, 1987) -- even aside from the fact that there are more schizophrenic mothers among this group of parents. Some of the non-schizophrenic mothers also tend to show similar interactions. Massie and Rosenthal, in their systematic blind observations of the home movies of mother-infant interactions prior to the referral of the infants for psychotic illness, found differences in the way the mothers held their babies and oriented toward them.

As children grow older they must adapt to the social environment outside the home (some perhaps already at a disadvantage due to their early history). The peer group becomes naturally a very important part of the child's environment at
this time. One might expect that the high-risk children find social adjustment more stressful than other children. Evidence that this is the case can be seen in the fact that, already in elementary school, their peers rate them as less competent than other children (Weintraub et al., 1978). Deviance in the children's speech patterns (Harvey et al., 1982) may make communication with both peers and adults more of a problem as well. Evidence for speech dysfunction similar to that found among schizophrenics was found in the Stony Brook high-risk sample when the children's speech was examined using the Rochester and Martin technique for the analysis. School itself may prove more difficult for such children because, as we have already noted, they show impairments of attention which increase with age (Erlenmeyer-Kimling et al.)

Moving on into adolescence, the social environment remains a problem, as Kreisman ( ) discovered when she found that schizophrenics had had difficulties making close friends with whom they could share intimacy at that time. And finally, one might expect that environmental stress should be greatest in late adolescence when the structured settings of home and school give way to the responsibilities entailed in living more independently, holding a job, and establishing a family. The concatenation of environmental stresses at this stage, cumulated behavioral and biological deviance, and perhaps the neurological evidence of changes (Feinberg's work?) during adolescence might serve as a sufficient trigger for the increased onset of schizophrenia at this age.
One more point needs to be made about the environmental impact, and that is that some environmental factors such as the social network or ecological niche may serve to protect a person at risk. The structure of early childhood settings, having mothers who are somewhat older and better educated, who work and have help with child care (Goodman, 1987) all seem to mitigate the occurrence of symptomatology among high-risk children. In the Finnish study (Tienari et al., 1987), it was clear that the high-risk children who were adopted into poorer functioning families fared worse than the high-risk children adopted into better functioning families.

Thus there appears to be some evidence that the environment can play a mitigating as well as an aggravating role in the occurrence of severe psychopathology and specifically in the onset of schizophrenia.

Summary

We have described the variety of scientific models for the etiology of schizophrenia and have suggested a superordinate model - the vulnerability model - to encompass all of them. We have indicated that the developmental model can serve as another superordinate model providing the time framework for the development of both normal and deviant individuals. It was further pointed out that in searching for indicators to identify the vulnerable individuals we have two classes - the wired in variety probably genetically transmitted and the neuroplastic part of the brain in which the post-evolutionary responses are
developed that are transmitted culturally and that are therefore more difficult to identify now.

The goal of the identification of the vulnerable is to try for prevention. It is clear that the inheritance of a vulnerability as well as its environmental acquirement do not necessarily and inevitably lead to the development of the disorder. If we could identify the vulnerable, it would become possible to launch educational strategies and prophylactic techniques for prevention of both the initial episode as well as recidivism. Such strategies and technique have been effective with people vulnerable to diabetes and following this paradigm we may also succeed with schizophrenia.

It should be pointed out that the studies incriminating parenting as potential factors in the development of episodes of illness do not necessarily claim that deviant parenting is the cause. It is more likely a trigger; and environmental triggers can be kept from firing the gun by proper education and prophylaxis.

There are now two reigning types of models - the disease model and the vulnerability model. The developmental model can be encompassed by either of them or by both. But how do they differ? The conventional view of the disease model regards the patient as essentially a sick person with intermittent periods of remission but with a high risk of eventual chronicity and deterioration. The vulnerability model regards the patient as essentially a healthy person with intermittent episodes of illness but with a high probability of eventual return to a
premorbid state of health. The essential difference between these two points of view is "hope", and what a difference this can make in the treating clinician.