Implications of the Vulnerability Model for DSM IV

With Special Reference to Schizophrenia

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Introduction

It is generally agreed that DSM III is atheoretical, steering a midcourse between the Scylla of theory and the Charybdis of practice. Despite this precarious balance it is hoped that DSM III will improve clinical practice by tightening the definitions of the categories of disorder, and will also improve research by specifying the characteristics of patients included in research designs so that replication becomes possible. However, if further progress is to be made, we must eventually incorporate the diagnostic schema into a theoretical structure. The purpose of this chapter is to review some of the more fruitful theoretical models that are now operative and try to integrate them into a superordinate vulnerability model that will incorporate the findings of each of the disciplines contributing to psychopathological knowledge. Methods for identifying the presence of the various specific disorder categories, based on the parameters of the vulnerability model, will be suggested as a new axis for DSM IV. Before presenting this new axis, we shall briefly review the status of DSM III from this new perspective.

Reliability

The first step in any classification schema is observation of the phenomena in the area of interest. Such observations have accumulated in psychopathology over the last 34 centuries; the specific phenomena of psychopathology observed by our predecessors form the matrix from which are drawn the specific symptoms, signs syndromes, and individual items of psychopathology that constitute our various classification instruments (DSM III, RDC, PSE, SADS, etc.). The standardization of these instruments has increased the reliability of our diagnoses but has left validity relatively
untouched. Thus, we are in the position of having developed a new, reliable thermometer, but do not yet know what it indicates.

Even the reliability of the new instruments has been called into question, since the individual items and symptoms of psychopathology have not yet been defined sufficiently to insure that different interviewers have the same criteria in mind when deciding whether a given symptom or sign is actually present. We need research criteria for the individual items similar to the research criteria for diagnosis. Wing [Wing74] and his colleagues have gone a long way in providing such definition for many items in the glossary of their manual for the PSE, but much still remains to be done.

To achieve this, we need to lay aside our rating scales and interviews once in a while and observe the patient the way our predecessors did, and, in the process, provided us with phenomenological observations which we have codified into our interviews. But we cannot rest on their laurels -- otherwise, psychopathology will be crystallized as of 1983 -- and go no further.

Are Rigorous Definitions Required?

One of the hopes of the authors of DSM III was to introduce more rigor in the definition of the categories in the nomenclature. But is it necessary that a category be defined rigidly in a close-ended way, like a mathematical concept? If this were necessary, such a widely useful concept as "species", for example, would go by the board, as Julian Huxley [Huxley40] has pointed out.
If biologists cannot define species rigorously, we need not be shamefaced that we cannot rigorously define schizophrenia, or for that matter, mental disorder itself. The test of a good definition is not ironclad rigor, but usefulness.

For the scientists who are interested in the disorder and its causes, approximate open-ended definitions are sufficient, since they are continuously testing and probing the borders of the definitions and extending them or contracting them as the facts warrant. For the clinician interested in the individual patient about whom decisions need to be made, a specific diagnosis is necessary, and that is why the RDC are so necessary even though they are still in the research stage.

Validity

We cannot be satisfied with reliability alone -- we must also ask whether our judgments are valid. Of the four types of validity -- predictive, construct, concurrent and content (MacCorquodale and Meehl, 1948; Cronbach and Meehl, 1955) -- we will deal only with the first two -- predictive and construct validity, since concurrent validity is really a type of reliability, and content validity refers to whether the measure covers adequately the entire area under investigation.

1. Predictive validity:

Outcome and course of the disorder provide criteria for the predictive validity of the diagnosis. Thus, if the diagnosis of affective disorder leads to a more rapid release than the diagnosis of schizophrenia, this can be taken
as a vindication of the diagnosis since this is the outcome we would expect. The narrower definition of schizophrenia, according to DSM III, for example, may indeed lead to a greater homogeneity in outcome in the category of schizophrenia as well as in the complementary category of schizophreniform psychosis. It would be expected that many patients with the strict definition of schizophrenia required by DSM-III would tend to have a poor outcome since chronicity is built into the definition of strict schizophrenia and similarly, many of the schizophreniform patients would tend to have a good outcome since they comprise individuals who have not yet, or are not likely to, become chronic. But, the results are not uniform for all the patients. There must be additional forces at work in the production of good and poor outcomes over and above the diagnostic label.

2. Construct validity: Scientific Models of Etiology

What else do we expect patients in a given category to have in common besides similarity in outcome? These expectations constitute the constructs whose validity is sought. They have been embodied in a set of scientific models for etiology that have been classified in two domains: field theory domain consisting of the ecological, developmental and learning theory models, and the molecular or biological domain, consisting of genetic, internal environment and neurophysiological models (Zubin, 1972). Each of these models leads to certain expectancies or hypotheses and these have been postulated elsewhere (Zubin, 1972). Here we will give only brief examples of these expectancies.

Accepting the genetic model, we would, for example, expect the most valid
diagnostic system to be the one which showed the highest transmission rate of schizophrenia in relation to consanguinity or the highest concordance rate in identical twins. A comparison of several diagnosticians (American, British and Swedish) was made in the Gottesman and Shields twin study, and the highest concordance rate was found in Essen-Moller's diagnoses (Gottesman and Shields, 1972).

Accepting the ecological model, we would for example, expect to find the highest rates of schizophrenia in individuals occupying the deprived, isolated, and oppressed ecological niches in our cities — and this indeed turns out to be the case.

Accepting the developmental model, we would for example, expect the highest rates among those who, according to Sullivan, and later verified by Kreisman (Kreisman, 1970), never had a close or intimate friend, i.e., had deviant friendship patterns in their adolescence.

Accepting the learning theory model, we would expect that families with deviant rearing patterns and individuals with negative reinforcement histories would give rise to more psychopathology.

Accepting the internal environment model, we would expect to find biochemical indicators such as monoamine oxidase differentials in schizophrenics and their relatives.

Accepting the neurophysiological model, we would expect to find deviant patterns in the processing of information input reflecting deviation in
attention and arousal. These hypotheses have been tested by such techniques as reaction time, sensory integration, pupillography, skin conductance and evoked potentials.

The recent discoveries in brain structure and function arising from the use of X-ray transmission scanning (CAT scans), positron emission tomography (PET), and nuclear resonance (NMR), have given neuropathology a new lease on life. It is to be expected that differences between patients and normals would be found in the anatomy and physiology of the brain by means of recent advances in the technology of brain scanning (Buchsbaum and Haier, 1983).

Each of these scientific models would require some modification of our diagnostic procedures in order to provide data for the construct validity of the diagnosis. Thus, the genetic model would require more careful interviewing methods of blood relatives to determine family incidence of mental disorder. The ecological model would require a more careful examination of the ecological niche the person occupies, stressing not only the generally accepted parameters such as socioeconomic status, crowding, etc., but also the more subtle aspects of available opportunities for growth, privacy, etc., and their frustration. The developmental model would place more emphasis on premorbid history and the learning theory model would require more careful surveys of reinforcement contingencies in the family, at work and in leisure situations. The internal environment model would require a careful survey of body chemistry and metabolism along the lines dictated by recent findings, while the neurophysiological model would require the application of information processing theory with the specific laboratory techniques found to be differential between patients and normals as well as between patient
groups. The application of brain scanning techniques would provide a more reliable method for detecting organicity as well as provide differential diagnosis between various categories of mental disorder.

While these studies are still in status nascendi, it would be well to include an appendix to DSM IV, which would present the results of such studies in the form of an additional axis - a vulnerability axis. If this is done, it may be possible that DSM-X or some earlier version eventually will have included in its main body the results of this axis. These results, however, cannot come from large scale studies, but must depend upon carefully conducted small scale studies before they can become part of our corpus of certitude.

Vulnerability Model

That the various etiological models do not exist in isolation is so apparent that it hardly needs mention, despite the fact that many researchers as well as laboratories often ignore this fact. In order to provide an integrating model that would include the seven etiological models, a supraordinate vulnerability model has been suggested (Zubin & Spring, 1977). It consists of the following assumptions:

1. Schizophrenia occurs in vulnerable individuals when they are subjected to sufficient stress and strain environmentally through their life events or endogenously through their biochemistry which may also be triggered by environmental life events.

2. When the stress induced by the life events surpasses the threshold of vulnerability, an episode develops, unless certain moderating variables absorb the stress and protect the individual, thus preventing the episode from developing. Notable among these moderating variables are the social network, ecological niche and premorbid personality.

3. The episode ends when the stress subsides and the person returns to his premorbid level of adjustment, or nearly so. Since the
occurrence of an episode is an overwhelming experience, there is a
great likelihood that certain residual effects may persist.
Whether these effects are to be attributed to schizophrenia itself,
or to iatrogenic, nosocomial or ecogenic influences independent of
schizophrenia is still unknown. Such factors as inability to find
a job or loss of friends because of being labelled schizophrenic
may be tangential rather than direct influences of the disorder.

4. If the premorbid level was satisfactory, the person is regarded as
recovered -- this is why good premorbid tend to do well.

5. If the premorbid level of adjustment was precarious (but not
psychotic), the person may be regarded erroneously as still
unrecovered -- this may be the reason why poor premorbid tend to
be regarded as doing poorly.

To summarize, the only permanent characteristic of the schizophrenics is
their vulnerability; their episodes are transient.

Chronic Schizophrenia

One of the most controversial aspects of the new view regarding the
vulnerability approach to mental disorders, especially schizophrenia, is the
question of chronicity. If schizophrenia is an episodic disorder, how can we
explain the apparent frequency of chronic schizophrenics? Is chronicity an
artifact, or is it a natural sequence in the course of the disorder?

Though the incidence of chronics is relatively small, they accumulate
over time to yield a high prevalence. Even of those appearing to be chronic,
some 30%, according to Bleuler's (Bleuler, 1978) data, remain needlessly in
the hospital because they have nowhere else to go. Is it possible that
chronic schizophrenia could be a psychosocial artifact caused by the
psychosocial consequences of acute attacks of illness rather than a natural
sequence in the development of the illness? The symptomatology of
schizophrenia can be classified into positive and negative categories (Wing,
The acute schizophrenics are characterized by largely positive symptoms and the chronics by mostly negative symptoms even though some patients possess both types of symptoms. Positive symptoms refer to the presence of overtly deviant characteristics, e.g., hallucinations, delusions, thought disorder, incoherent speech and other florid symptoms. Negative symptoms refer to the absence of behavior expected in a normal individual: capacity for emotional involvement, activity, drive, speech, social interaction, clarity of thought and movement, attention to personal appearance, self-support, psychosexual inclinations, and other socially expected responses. Deviations in these normally expected behaviors constitute the clinical poverty syndrome. But are these negative symptoms necessarily the result of schizophrenia? First, these negative symptoms may have characterized some of the individuals in their premorbid status, and, it is no surprise to find these traits still present after the episode ends. About 70% of the schizophrenics in Bleuler’s (Bleuler, 1978) data fall into this category. Some of these negative symptoms may be prodomal, appearing in the incipient stages of an already developing episode. It is often difficult to differentiate between premorbid characteristics and prodromal characteristics. From the point of view of vulnerability theory, there is no need to make this differentiation, since it is likely that the prodromal symptoms would disappear with the end of the episode and only the premorbidly based characteristic would remain.

Furthermore, there is a group of patients whose deviant behavior may have developed while in the hospital. If such behavior persists after their discharge, it is mistakenly regarded as the residual consequence of the
disorder rather than merely of incarceration.

We had thought that we were alone in regarding chronic schizophrenia as an artifact and perhaps as a temporary aberration which may eventually disappear if proper preventive methods are applied. To our surprise, Professor Luc Ciompi (Ciompi, 1980) contends, as we do, that chronic schizophrenia could be mainly a psychosocial artifact caused by the psychosocial consequences of acute attacks of illness.

Ciompi argues as follows: most of the negative symptoms reflect hospitalism and institutionalism. They occur not only in mental hospitals but in prisons, understaffed nursing homes and wherever monotony and stimulus deprivation obtain, and often disappear under stimulation. These negative symptoms are not limited to schizophrenics and it is often difficult to tell in the long-term wards what the diagnosis of the ward residents originally was.

A more detailed analysis of the nature of negative symptoms leads to the problem of the etiology and fate of negative symptoms. The most generally accepted notion about negative symptoms is their persistence, that is why they have tended to become associated with chronic schizophrenia. But has the permanency of negative symptoms been established?

One strategy, advocated by Will Carpenter (In Press) and others is to try out a variety of strategies to eliminate, if possible, the negative symptoms since they seem to be the big stumbling block in the recovery from chronicity.

Depending upon the probable source of the negative symptoms, the following strategies are proposed:

1. If the positive symptoms are a response to the psychosis resulting from
self-preoccupation or from a defense maneuver to dampen its impact, they should generally disappear with the recovery from the episode provided they have not been stamped in by nosocomial and/or iatrogenic influences.

2. If they are induced by drug treatment (akinesia, sedation) a change in the treatment regime seems indicated.

3. If they reflect the understimulation which Wing and Brown (1970) found to be the case in many instances, they can be eliminated by environmental manipulation.

4. If they are induced by the acute psychotic episode or post episodically, proper therapeutic intervention should be found by clinical trial and error.

5. If these strategies fail to eliminate the negative symptoms, they could be regarded as genuine aspects of the schizophrenic process which gives schizophrenia its chronic characteristics. However, before accepting this conclusion it would be of interest to determine whether these negative symptoms are not a reflection of the premorbid personality characteristics.

The data from the three European follow-up studies (Bleuler, 1978; Ciompi, 1980b; Huber, Bross, Schuttler & Linz, 1980) indicate that the general trend for schizophrenia is improvement rather than deteriorative chronicity, and if there is a true course for schizophrenia it is an open life process rather than a unidirectional disease process, with general improvement and even in some instances eventual cure rather than deterioration: witness the sporadic recovery of patients even after a lifetime of chronicity.

The long term outcome of schizophrenia is often independent of genetic influence as measured by the presence or absence of family history of
Schizophrenia. This is in contrast to the acute onset of the illness which shows a relationship to family history, though not invariably. Since genetics does not relate to chronicity, environmental factors must be operative.

There is evidence for the association of chronicity and relapse with such psychosocial factors as life events, labelling, highly critical families, but very little association with psychopathology and diagnosis. The iatrogenic, ecogenic and nosocomial aspects of psychosocial factors have sufficient influence to maintain the state of chronicity or produce relapse. Modern family research, despite the heterogeneity of its methodological approaches, consistently shows that family-dynamic factors play a role in the prolongation and resumption of schizophrenic states.

There is still no generally accepted evidence today of any type of somatic biochemical or other organic basis for the chronicity of schizophrenia, though there seems to be preliminary tentative evidence of such etiology for the acute, albeit, transient, characteristics of the early phase of the illness.

After presenting the arguments in favor of considering chronicity as an artifact, Ciompi proceeds to list the counterarguments of those who regard chronicity as an essential element in the schizophrenic disorder and not an artifact. He doubts the validity of these counter-arguments and gives his reasons for their invalidity. First, the existence of irreversible residual

1 The evidence from CAT scans and PET scans is still not specific to schizophrenia.
states or negative symptoms would argue for chronicity. In response, Ciompi points out that irreversibility may develop as a result of environmental influences and not necessarily as a result of persistent, functional or organic disorder. The sporadic recovery from long enduring chronicity contradicts the irreversibility hypothesis.

Secondly, the possibility of the biochemical or organic basis for chronic schizophrenia has to be considered. This argument is negated by the fact that chemical intervention is effective in acute schizophrenia with its positive symptoms, yet seems to be ineffective on the negative symptoms. These may require psychosocial intervention. This raises the question of whether the negative symptoms are an essential part of the schizophrenic disorders. There is a possibility that the negative symptoms may not be a reflection of the morbid state of schizophrenia but may instead reflect the premorbid characteristics of the individual or his postmorbid or residual symptoms induced not by the disorder but by the side effects of the disorder - labelling, self-derogation, inability to obtain jobs etc.

Third, it is sometimes difficult to differentiate between chronic and acute schizophrenia, since the former sometimes retain the positive symptoms alongside the negative ones. This counterargument is not easily resolved and until the differential diagnostic problem of separating acute from chronic schizophrenia is solved no conclusion can be reached. It has occurred to the present writer that there is a great likelihood that there exists a small group of patients (estimated at no more than ten percent in Bleuler's (1972) data) who appear to be continuously in an episode, and are continuously hospitalized. These may be individuals who are so vulnerable that even the
usual everyday stress that the human condition is subject to, is sufficient to trigger a series of rapid episodes with only brief, perhaps unnoticed, intervals of normality between them. These may be the individuals in whom the positive and negative symptoms come into play; the positive items reflect the onset, and the negative, the after-effect of the brief episode. There is, of course, the possibility that a small proportion of this ten percent is permanently chronic due to excess internal secretions or some other causal agents.

The fourth and final counterargument concerns the ubiquity of chronicity. Does this mean that chronicity is independent of the environmental influences that have been postulated? It is difficult to answer this question, but until it can be demonstrated that all the psychosocial factors can be dismissed as ineffective, the ubiquity argument cannot be decisive. Furthermore, this ubiquity is not uniformly distributed across cultures and, hence, most likely subject to environmental influences.

In summary, Ciompi's arguments and counterarguments, as well as those of the author, lead to the conclusion that the hypothesis that chronicity is an artifact is not negated and may be a tenable view to take. All in all, these arguments help buttress the claims that chronicity is not a natural, inevitable outcome of schizophrenia anymore than that poverty is a natural outcome of physical disorders.

It will become necessary to develop methods for insuring that the small group of possible chronic schizophrenics satisfy the criteria for the continuous presence of the episode and are not pseudo-chronic. In other words, we need not only markers of vulnerability but also markers that determine the
boundaries of episodes. How this is to be accomplished is a matter for further research.

Treatment

Another problem which is not yet within the framework of DSM-III is the role of treatment in diagnosis. Since one of the chief purposes of diagnosis is selection of treatment, the role of diagnosis in the selection of a specific therapy from the ever increasing number of options is a crucial aspect of the classification system and may require a special axis.

Perhaps the most prevalent treatment is the chemotherapeutic approach, and it is well recognized that neuroleptics and chemotherapy in general are not a "cure" in the sense that say, antibiotics cure infections. If the function of neuroleptic treatment is not "cure" but "mitigation" by raising the threshold for the impact of life-event stressors (or for the impact of the drop-off in the reinforcements required to maintain homeostatic coping ability) (Salzinger, 1980), it becomes clear why relapse occurs even under complete compliance with the drug regime. The blood level of the neuroleptic corresponding to the prescribed dosage may become too low to provide the protection against the impact of stress, or the traumatic impact of the stress (or drop in reinforcement frequency) may become so excessive that the protective nature of the dosage is no longer adequate.

The point to be stressed is not that the drug is needed to reduce psychotic manifestations, which are assumed to be continuously present and require continued suppression. Quite to the contrary. It is suggested that psychotic manifestations are not always present. These manifestations appear
only in response to life event stressors, and it is the consequent stress which they produce that is being contained by the drug treatment or other types of treatment. The view that psychotic manifestations fluctuate spontaneously or randomly may be a reflection of an older concept that schizophrenia has a natural course of its own which has to play itself out. A more careful monitoring of the course of illness may reveal the existence of ministressors of every day existence as well as the more dramatic maxistressors which account for exacerbation or relapse. Among these stressors are probably the side effects of the neuroleptic treatment itself, which also needs monitoring.

It is likely that just as chemotherapy can suppress or eliminate acute positive symptoms, psychosocial treatment can be utilized in the suppression, prevention or elimination of the chronic negative symptoms. This may lend additional evidence for considering chronicity an artifact rather than a natural aspect of the schizophrenic disorder.

**Difficulties in Diagnosing Mental Disorder**

Aside from a lack of specified criteria, which is being corrected by Research Diagnostic Criteria, there is an inherent weakness in diagnosing mental disorders, especially schizophrenia, because it is behaviorally or cognitively based and has no palpable somatic accompaniment as is often the case in physical disorders.

The behavior of mental patients is determined not only by their mental disorder but also by their underlying premorbid personality and the conditions under which they function and it is this combination of effects which is the
presenting picture at the time of admission. If we could separate the behavior due to the mental disorder from the behavior due to the premorbid personality and to their interaction, we could recognize the focal disorder (schizophrenia) in isolation and probably find this factor characteristic of all similarly afflicted patients. What we perceive, however, is not the effect of the focal disorder, but the effect of the illness, which reflects the premorbid personality itself and its interaction with the disorder. This is why no two schizophrenics are alike -- their focal disorder may be the same but their illness is different. The relation between premorbid personality and psychopathology is still moot and involves such thorny issues as the distinction between "trait" and "state", but it might be valuable to adopt the null hypothesis and study premorbid personality as an independent variable or set of variables. In fact, studies in Lund, Sweden (Hagnell, 1966) have found that the premorbid personality, as measured by the Sjöbring method, does not relate to occurrence of mental disorder, but does color it, once it appears. This is somewhat at loggerheads with the data on the same population when "lesional" aspects of personality were considered. Perhaps the Sjöbring personality variants lie essentially in the normal sphere and do not show the greater deviances that the "lesional" factors show.

It should be noted, however, that Gottesman and Shields (1972) found that 13 of 33 schizophrenics in their study of twins, or nearly 40 percent, were judged schizoid in their premorbid personality and nine more were regarded as otherwise abnormal, bringing the total of deviant personalities to two-thirds. This is in agreement with the proportions of premorbidly deviant personalities in Bleuler's (1972) study. It is of interest that the concordance in Gottesman and Shield's twin study of monozygotic twins (1972) was highest in
he pairs of monozygotic twins when the proband twin was schizoid and lowest when the proband was normal. It would be interesting to examine these data or see if when concordance vs. discordance are the independent variables, the difference in the proportion of schizoids is still significant. Where the proband twin was schizoid and lowest when he/she was normal.

However, a comparison of Bleuler's (1978) premorbid personality data for his schizophrenics with the distribution of primary personality (normal vs. lesional) in the Lundby study (Zubin, Magaziner, & Steinhauer, 1983) has shown that although there is a relationship in the general population between premorbid personality and the occurrence of an episode, it is rather weak. The risk for schizophrenia in the deviant primary personalities in the general population is nine percent compared to the risk of only 0.7% in the non-deviant. There must be other factors besides poor premorbid personality that facilitate the development of an episode in a presumably vulnerable individual, since only nine percent of the deviant primary personalities develop episodes while 91% do not. Thus, even if we limit ourselves to genotypes only for the etiology of schizophrenia and accept the estimate for penetrance at .25, we would expect 36% of the deviant personalities to be vulnerable, i.e., have the genotype, but only nine percent developed the phenotype. What protects the remaining unaffected 27%?

**Moderating Variables**

It is clear that vulnerability alone does not insure the occurrence of an episode. In order for an episode to occur in a vulnerable person, there is first a need for a sufficient amount of stress to exceed the coping ability of the person or overcome his capacity for homeostatic containment of the stress.
Once the stress threshold is breached, there are several more protective mechanisms that have to be overcome before the episode sets in. First is the social network surrounding the person. If it is sufficiently strong and supportive, the episode may be stillborn. Then there is the ecological niche the person occupies which provides physical, social and economic facilities which may abort an episode. Third, is the premorbid personality, which, if it is sufficiently well developed may provide the coping ability to ward off the episode. There are probably other factors that may also serve as moderating variables that may prevent or enhance the risk of the episode depending upon their strengths.

Heterogeneity of Diagnostic Categories

The method of classification in DSM III is polythetic rather than monothetic, since the RDC do not provide a homogeneous group for each diagnostic category. It is not unlikely that individuals in the same category may have no single criterion in common. This heterogeneity has led many workers to wonder whether schizophrenia is a unitary entity, or is composed of several subgroups. The advent of the drug era has also brought a search for subtypes of the various diagnostic categories based on similarity in responses to specific drugs. This has opened up a demand for clustering techniques which would identify the individuals belonging to each of the various homogeneous subtypes. The frequent failure to replicate such findings has resulted in the conclusion that blind empirical search for such subtypes without any underlying testable hypotheses was a vain attempt at lifting oneself by one's own bootstraps. Fleiss and Zubin (1969) have pointed out that we need better mathematical models for typology before wasting our time in unchartered courses.
Furthermore, the differences between the dimensional approach and the typological approach are often vitiated by the factor analytic approach used in determining the dimensions used in clustering, since factor analysis makes assumptions which nullify typological assumptions (Fleiss and Zubin, 1969). For example, typology thrives on non-linear relationships between variables and on discontinuous non-normal distributions, assumptions that are incompatible with factor analysis. Consequently, it is foolhardy to expect to find types when the assumptions they are based on are not compatible with the techniques used to find the types.

There is another point of view, however, which would indicate that the conflict between dimensionality and typology is ephemeral. It can be best illustrated by an incident during a prior conference in diagnosis (Katz, Cole and Barton, 1965). The same question had been raised then, 20 years ago, and the discussion had lasted till late in the evening. I couldn't fall asleep that night and waking at 4:00 a.m., I turned on the TV only to discover that I had tuned into the Farmer's Hour and was listening to a lecture on Pomology - how to tell good from bad apples! Apparently, the earlier method was to have an apple knocker tap the apple with his knuckles to determine whether it had too much water core and whether it was immature. Today, the reporter indicated, the method consists of conveying the apples on a conveyor belt under two sets of monochromatic lights. The amount of light absorbed is read off a dial which automatically determines the fate of the apple. Apparently, the typology of the apple knocker has been converted to a dimensional measure for classifying the apples. Upon further thought, I concluded that actually this dimensionality is probably the reflection of the genetic make up of the apple seed - again a typological classification into good and bad genes. But
genes accomplish their work by secreting certain biochemical substances (amino acids) in smaller or larger quantities. Again, the typological genetic classification has been altered to a continuous dimensionality. And so on.... Apparently, the state of the art determines whether typology or dimensionality is to be preferred for classification. Furthermore, mathematical techniques can probably be developed for converting a typological classification into a dimensional one, and vice versa. Thus, the taxonomy depends upon the state of the art, and until we are forced to do otherwise by the weight of the evidence, we can hold on to a unitary concept of schizophrenia, despite its heterogeneity.

Metamorphosis of Schizophrenia

In addition to the impact of the new discoveries in etiology, there has also been a growing, though not yet generally accepted, change in attitude towards some mental disorders, especially schizophrenia and the affective disorder. Among these changes are the following (Zubin, Magaziner, & Steinhauer, 1983):

1. Schizophrenia is becoming more benign in its outcome when compared to the outcome during the first third of this century -- only about 10% of schizophrenics remain chronic, 30% recover and return to the community, and 60% oscillate back and forth in their episodes.

2. Schizophrenics with good premorbid personalities tend to have good outcomes, while the poor premorbid have poor outcomes. This is one of the most stable generalizations in psychopathology and has held true since Kraepelin's days.

3. Sudden onset leads to good outcome while gradual insidious onset lead to poor outcome is another stable generalization.

4. Schizophrenics are not schizophrenic all the time and a good number have but one episode, and even those who have more than one episode are only intermittently sick, often returning to a well state between episodes.
5. The contrast between the medical model for mental disorders and the vulnerability model can be epitomized as follows: the medical model regards the patient as a sick person who has intermittent well periods. The vulnerability model, on the other hand regards the patient as an essentially healthy individual who has intermittent episodes.

These five factors have led to a veritable Kuhnian paradigmatic revolution in our thinking about schizophrenia. "Once a schizophrenic, always a schizophrenic," no longer is tenable, but what does differentiate the schizophrenic from others?

Markers of Mental Disorders

To test the validity of the vulnerability model, it becomes necessary to develop markers that would identify vulnerable individuals. In order to make such identification, it is necessary to discover certain characteristics that would serve as earmarks of vulnerability.

As used here, "markers" refers to specific types of performance or characteristics that identify individuals who either had a schizophrenic episode in the past, are having one presently, or have a high risk of developing an episode in the future. Ideally such a marker should be present only in those vulnerable to schizophrenia and not to any other mental disorder.

Table 1 shows the status of the various types of markers by their pre-episode, episode and post-episode status (Zubin & Steinhauer, 1981). Three types of markers are presented.
1. **Vulnerability markers (A, AA, D).** In order to qualify as a vulnerability marker, it should be present in the pre-episode, episode, and post-episode periods, and should also be present in greater frequency than chance in unaffected siblings. There are several types of vulnerability markers. A satisfies all the requirements for a vulnerability marker. AA is a marker which is present during all the three specified periods but is not characteristic of siblings, and hence is probably non-familial. D is a vulnerability marker which disappears after the episode ends but nevertheless is found in siblings. Apparently the episode extinguishes the marker.

2. **Episode Markers (B).** This marker is present only during the episode and does not characterize unaffected siblings. The starting point in the search for episode markers is to assess the individuals who have already exhibited their vulnerability by having had, or are presently having, an episode. Once the marker is found, it may be applied to the general population to identify those who are undergoing an undetected episode or in the case of a vulnerability marker, those who are vulnerable (possess the marker) but have not yet, or never will, develop an episode. The episode marker can also be useful in patients undergoing an episode to determine whether the episode is still active or has terminated, since the episode marker waxes and episode, it is difficult to determine without suitable follow-up or follow-back, whether the marker under investigation is an episode marker or a vulnerability marker. To differentiate between the two types of markers, the status of the marker must be known in the pre-episode period, during the
episode, and post-episode.

3. **Residual markers** (E, G). These markers may make their appearance during the episode, but persist after the episode. Whether they are indigenous to the disorder or are the result of iatrogenic, nosocomial or ecogenic factors is still unknown.

In addition to these three types of markers, there are certain prodromal characteristics which usually appear when an episode is imminent. However, these prodromal characteristics are not always followed by an episode and hence, cannot serve as markers, but as predictors of a possibly approaching episode.

4. **Invulnerability markers**

The HH marker, which is present in siblings of schizophrenics but absent in the probands themselves presents an interesting possibility. Perhaps an HH marker is an indicator of invulnerability, a characteristic which is antithetical to schizophrenia even as Meduna thought epilepsy was. Similarly, the AA marker which is absent in siblings in a proportion significantly below the general population, but is present in the probands in pre-episode, edisode and post-episode intervals, may identify by its absence the individuals who are resistant to schizophrenia. A search for such markers would indeed be a worthwhile endeavor.

**Markers and Information Processing**

The search for markers of psychopathology had previously been erratic and unsystematic, based primarily on hoped-for serendipity. For a more productive approach, the search should be guided by an overall rational strategy rather
than by trial and error. Although there are no criteria for selecting the most suitable strategy, the information-processing approach has found favor in many laboratories. The reason for this choice is based on the assumption that the deviant behavior observed in psychopathology may arise as a result of impairment or deviation in the information-processing capacities of an individual (Kietzman, Zubin, & Steinhauer, 1983). Now, in the pre-information processing days, I would have been delighted to find a differential between patients and normals and add this differential to the repertoire of previous findings. From the point of view of information processing, the finding of a difference is now only the starting point. It becomes important to know just where, when, and how the differences developed in the pathway between the input of the stimulus and the emergence of the response.

Information processing consists of the manipulation of symbols and patterns (Simon, 1979) generated either endogenously (by, for example, attention) or exogenously (from stimulation by the environment), which are stored and subsequently built into more complex structures. While the basic elementary operations underlying the global manipulation of symbols and patterns are not yet well understood (Posner, 1971), it is becoming clear that such processes as pattern recognition and comparison, preattentive processes and primary automatic processes constitute important examples of information processing. Since one of the prevalent theories about the nature of schizophrenia and other mental disorders is that they are based on a cognitive dysfunction, or failure, at least in part, to deal normatively with symbols and patterns, it is understandable why we turn to information processing in our search for markers for schizophrenia.
The information-processing approach delineates different stages in the pathway between stimulus and response. The basic notion is that all behaviors, even the simplest, pass through these different steps or stages and that by focusing upon specific stages one is actually emphasizing different types of behaviors, e.g., perception, memory, and so on. Occurring simultaneously with the behaviors of the different stages are other endogenous events or processes, which are viewed as controlling the ongoing processing activities, e.g., attentional factors which are known to have an influence on behavior.

Since mental activity must somehow be based on, or related to, brain activity, it becomes necessary to build a bridge between the two if we are ever to fully understand information processing. For this reason, we deal separately in our search for markers with, on the one hand, the manipulation of symbols and patterns which constitutes the flow of information, and, on the other, with some of the possible parallel metabolic or neurophysiological correlates of the symbols and patterns. This approach which has developed in normal cognitive psychology has now begun to be applied to psychopathology. It is similar to the analogy that has been made between computer processing and behavioral processing, with a strong emphasis upon delineating various stages of processing, identifying the components presumed to be operating at these various stages, and exploring the role that endogenous events and processes (called control processes) have upon the stages and components of processing. The purpose of information-processing research is to elucidate the various stages and control processes. Once it is possible to systematically describe and explain behavior in terms of stages and processes, we can consider how the different stages and processes are interrelated.
Such knowledge could be used to explain complex behavioral reactions and responses in psychopathology.

**Psychoses vs. Personality Disorders**

Another problem that the vulnerability model addresses is that of the difference between the precision in the definition of DSM III categories in the functional disorders as compared to the more diffuse imprecision in the neurotic and personality disorders.

The functional disorders are characterized as states (episodes) which wax and wane. The only persistent trait in such cases is vulnerability, which is more or less a permanent characteristic of the individual. In the personality disorders, we deal with a persistent behavioral trait which is a permanent characteristic of the individual, and though it may be exacerbated or mitigated by life events and contingencies, the disorder itself is a persistent trait of the individual. The same probably holds true of neurosis. For this reason, these three conditions cannot be treated in the same way. Thus, we can expect complete recoveries in the functional disorders when the episode ends, but not to the same extent in personality and neurotic disorders, unless these long lasting imbedded traits can be eliminated.

**Implications of the vulnerability model for DSM IV**

With regard to predictive validity, the differentiation between the more narrow concept of schizophrenia in DSM III and the previously held wider concept has led to a more severe outcome for the narrower definitions. thermore, the outcome in developing countries (World Health Organization,
1979) seems to be better than in developed countries. However, not all the narrowly-defined schizophrenics fail to improve, and not all the schizophreniform patients tend to improve. Furthermore, not all the patients in developing countries do well on follow-up. The vulnerability model, in contrast with the medical model, introduces the concept of triggering life events as a necessary precursor of an episode in a vulnerable person and further provide for moderating variables to abort an episode even if it is incited by life event stressors. These factors may explain the recurrence of episodes or their non-recurrence on follow up. Thus, by considering the disorder as episodic, to be triggered by external or internal stressors, and by considering the role of moderating variables in the production or abortion of new episodes, the contradictions in outcome do not appear as imponderable. This model also explains why not all the good premorbid personalities fare well in outcome and not all the poor premorbid personalities fare poorly. Other moderating variables such as social networks and ecological niches need to be considered.

The implication of the vulnerability hypothesis is that our diagnostic studies need to regard schizophrenia as some type of allergy and try to discover the contingencies that elicit it. In fact, a study of these contingencies could become the basis for a new type of diagnosis based on a behavioral analysis as Kanfer and Saslow (Kanfer and Saslow, 1965) have done. To this end we need measures of vulnerability to schizophrenia as well as markers for the beginning and ends of episodes. Armed with such indicators, we may be able to take the next giant step -- that of preventing the vulnerable from developing even a first episode. To this end, we need to develop criteria that would serve for screening markers in the general
population. Only in this way can we find the vulnerable, and once detected, afford them preventive guidance.

Potential Vulnerability and Episode Markers

The potential markers for mental disorders were recently reviewed by several authors (Zubin & Steinhauer, 1981; Zubin, 1979; Usdin & Hanin, 1982). There seems, therefore, no need to add another review at this time, especially since progress in this field is not very rapid.

A dispassionate view of the marker field leads one to the conclusion that, at the present time, there are no markers specific to a given category of disorder but there seem to be markers that occur more frequently in the mentally ill during their episode and some of them also occur in a significant proportion of unaffected relatives. In developing a vulnerability axis, it becomes necessary to suggest which are the most promising markers at this time. In a previous publication (Zubin & Steinhauer, 1981) it was suggested that a useful classification of markers is provided by the etiological models from which they spring. Thus, the etiotype of the genetic model is the genotype, and each of the other models give rise to their specific etiotypes. Table 2 shows the distribution of potential vulnerability markers by etiotype.
### TABLE 2

Potential Vulnerability or Episode Markers by Etiotype

<table>
<thead>
<tr>
<th>Model Type</th>
<th>Etiotype</th>
<th>Potential Vulnerability or Episode Markers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic</td>
<td>Genotype</td>
<td>Consanguinity, HLA (human Leucocyte antigen typing)</td>
</tr>
<tr>
<td>Ecological</td>
<td>Ecotype</td>
<td>Migration, social marginality, socioeconomic status, social isolation, emotional milieu of home, deviant social network</td>
</tr>
<tr>
<td>Developmental</td>
<td>Auxanotype</td>
<td>Season of birth (winter), postnatal cerebral damage, ophthalmological defects in probands and relatives, absence of intimacy in adolescence</td>
</tr>
<tr>
<td>Learning theory</td>
<td>Mathetotype</td>
<td>Severe communication disorder, inability to develop adaptive behavior or benefit from past experience, inappropriate reinforcement, reaction time crossover index, cross-modality index</td>
</tr>
<tr>
<td>Internal environ-</td>
<td>Chemotype</td>
<td>Levels of monoamine oxidase, dopamine-beta-hydroxylase, red blood cell catechol-o-methyl transferase, serum creatinine phosphokinase, platelet monoamine oxidase activity</td>
</tr>
<tr>
<td>mental</td>
<td></td>
<td>Pupillary response, smooth pursuit eye movements, event related potentials</td>
</tr>
<tr>
<td>Neuro-physiological</td>
<td>Neuro-physiological</td>
<td>Dilated ventricles, muscle anomalies, cerebral blood flow anomalies</td>
</tr>
</tbody>
</table>
Since the publication of this table, several additional markers have come to the fore. Among these are the Continuous Performance Task (CPT) (Kornetsky & Orzack, 1978), Span of Apprehension (Asarnow, Steffy, MacCrimmon, & Cleghorn, 1978) and Dichotic Listening with distraction (Spring - personal communication).

In connection with episode markers, it is important to note that in addition to utilizing follow-up studies to monitor the waxing and waning of episode markers, there is also a more direct route for determining immediately the presence or absence of an episode. This consists of challenging the individual with either a biochemical or a behavioral challenge, even as the presence of diabetes can be determined by the challenge of the glucose tolerance test. Janowsky and his colleagues (Janowsky, Davis, Huey, & Judd, 1979) have proposed the Ritalin challenge test for this purpose and van Kammen and his colleagues (van Kammen, Bunney, Cocherty, Marder, Ebert, Rosenblatt, & Kayner, 1982) have utilized the amphetamine challenge test. These challenges tend to exacerbate the clinical manifestations if the patient is still in his episode, but fail to do so if the episode is over.

The dexamethasone challenge test for depression is another way of probing for the presence of an episode. It is to be hoped that the tremendous effort now being exerted in the validation of these techniques will result in a useful group of reliable and valid instrument which could provide the basis of the vulnerability axis.

One type of behavioral challenge for probing the presence or absence of an episode, suggested by Alex Zautra (personal communication) can be useful
not only in probing but also in therapeutic strategies. Zautra divided schizophrenic patients into two task groups. One group was given the task of behaving in such a manner that the ward personnel would tend to favor their release from the hospital, while the other was given the task of behaving in such a manner that the staff would not countenance release. Some of the patients in the latter group reported when instructed to be ornery, that they were in fact already behaving in a way which was likely to keep them in the hospital. Having become aware of their ornery behavior, to their own surprise, as well as to the surprise of the staff, turned about face and began to demonstrate their release worthiness. Apparently, many patients automatically continue their maladaptive behavior even after their episode has ended. A challenge of the type described here might serve to disturb and disrupt the maladaptive routine and indicate that the episode has passed (i.e., an episode marker) in addition to providing a therapeutic strategy.

SUMMARY

The purpose of this chapter has been to provide the tentative beginnings of an additional axis for DSM IV. As Rue Cromwell (Cromwell, 1982) has pointed out, eight decades of exclusive devotion to symptomatology-based diagnoses is enough! We need to add the evidence for markers stemming from etiological investigations as an independent basis for making diagnoses. The search for markers which the vulnerability hypothesis has set into motion may provide the underpinnings of the vulnerability axis. The introduction of a systematic approach for discovering these markers under the general paradigm underlying information processing may yield a series of markers of the vulnerability, episode, residual or prodromal type which may provide the cutting edge for more homogeneous categories in our nosology. Furthermore, by
epidemiological studies of the general population, the vulnerable individual may be detected even before the first episode strikes. Cases of undetected disorders may be found by the testing for episode markers, and evidence for past episodes can be revealed by testing for residual markers. The imminence of an episode may be detectable by the search for prognostic as well as prodromal factors. Thus, the proposed new axis, when fully developed, ought to provide a new systematic approach which may buttress present nosology by more objective evidence, or provide new categories or subtypes which describe new but more homogeneous entities.

To accomplish this goal, a veritable academy of interdisciplinary colleagues is mandatory. One way of hastening the accomplishment of this approach is to convoke an academy of scientists covering the entire range of sciences dealing with the classification of human behavior, both normal and abnormal, to provide a taxonomy of behavior. Nearly all scientific fields deal with the problem of classification but most prominent in this area, in addition to taxonomy, are philosophy of science, anthropology, psychiatry, psychology, sociology, statistics and computer science. An academy of this type could serve the field of taxonomy even as the AcademieFrancaise serves the French language. It is clear that classification of mental disorders cannot be left to psychiatrists alone even as ichthyology can not be left to fisherman or navigation science to sea captains!
TABLE 1

Types of Markers by Pre-episode, Episode, and Postepisode Status, and Presence in Sibling

<table>
<thead>
<tr>
<th>Marker</th>
<th>Pre-Episode</th>
<th>Episode</th>
<th>Post-Episode</th>
<th>Sibling</th>
<th>Type of Marker</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>+*</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Vulnerability</td>
</tr>
<tr>
<td>AA</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>Vulnerability, nonfamilial</td>
</tr>
<tr>
<td>B</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Episode</td>
</tr>
<tr>
<td>BB</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>?</td>
</tr>
<tr>
<td>C</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>Vulnerability</td>
</tr>
<tr>
<td>CC</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>Vulnerability, nonfamilial</td>
</tr>
<tr>
<td>D</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>Vulnerability, normalized by episode</td>
</tr>
<tr>
<td>DD</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Vulnerability (nonfamilial), normalized by episode</td>
</tr>
<tr>
<td>E</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>Residual effect of episode</td>
</tr>
<tr>
<td>EE</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>?</td>
</tr>
<tr>
<td>F</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Vulnerability, normalized by episode</td>
</tr>
<tr>
<td>FF</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>Vulnerability (nonfamilial), normalized by episode</td>
</tr>
<tr>
<td>G</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>Residual effect of episode</td>
</tr>
<tr>
<td>GG</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>?</td>
</tr>
<tr>
<td>H</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Nondifferential for schizophrenia</td>
</tr>
<tr>
<td>HH</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>?invulnerability, non-familial</td>
</tr>
</tbody>
</table>

*Note: +, marker present; -, marker absent; ?, uncertainty whether pattern occurs in nature.

REFERENCES


