Vulnerability to Depressive and Schizophrenic Disorders—Conference Report

Abstract

A conference was held to foster improved research on vulnerability to psychiatric disorder. By bringing together groups studying vulnerability to depression and those studying vulnerability to schizophrenia, commonalities and differences across these two fields were clarified, and research approaches and problems were shared. Five major areas of particular importance were covered: (1) diagnosis and the assessment of function and intermediate clinical states, (2) statistical analysis and project design, (3) personality and family variables, (4) biochemical and physiological markers, and (5) comparison of vulnerability to schizophrenia and depression: models of causation and possibilities for collaborative research. Potential directions for increasing progress in the important area of vulnerability research were outlined.

There is good evidence that the major psychiatric disorders have complex etiologies. One important model for understanding these etiologies has been the studies of children who are considered at risk (vulnerable) by virtue of having one or both parents ill with the disorder. Such studies of "high risk" have generated a series of methodologies and findings.

Several years ago, the increasing number of investigations focusing on vulnerability to schizophrenia and the obvious complexity of the field led to the formation of a consortium where research groups could share their results and the problems in their studies. More recently, the multiplying efforts at studying vulnerability to depression also led to increasing contacts among investigators in this area. As research on vulnerability to depression and schizophrenia advanced, it became increasingly clear that the two endeavors might progress more effectively if conceptual models, methods, and findings were shared. To promote this sharing process, a group of investigators met in New Haven on March 23–25, 1983, to discuss findings, methods, and solutions to the problems of vulnerability research in depression and schizophrenia.

The conference at Yale was the first time investigators studying children at risk for schizophrenia and those studying risk for depression had met together. This conference, sponsored by the National Institute of Mental Health and the Yale Medical School Department of Psychiatry, had three goals: (1) to present basic findings, methods, and concepts in the fields of schizophrenia and depression vulnerability research; (2) to describe problems associated with this research; and (3) to explore the possibility for collaboration among investigators studying vulnerability to these two disorders.

This report synthesizing the discussions of the conference focuses on five major topics crucial to studies of vulnerability: (1) diagnosis and the assessment of function and of intermediate clinical states; (2) statistical analysis and project design; (3) personality and family variables; (4) biochemical and physiological markers; and (5) comparison of vulnerability to schizophrenia and depression: models of causation and possibilities for collaborative research.

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A list of conference participants follows this report.
Diagnosis and the Assessment of Dysfunction and of Intermediate Clinical States

The question of what is crucial to assess in vulnerability research is closely tied to basic conceptual orientations. To some extent, diagnosis is the only, or at least the major, crucial variable if one is merely attempting to establish a specific outcome for a given risk factor. If one wants to focus on evolving processes, however, and for the more efficient study of disorders such as schizophrenia with limited prevalence rates, the evaluation of intermediate clinical states, dysfunction in social competence, and even psychophysiological variables may provide clues to basic processes.

For these reasons, comparing differences of strategies between the two groups of investigators showed that those studying vulnerability to schizophrenia felt the need to broaden their assessment focus, while those studying vulnerability to depression tended to focus specifically upon diagnostic assessment.

In each of these endeavors, strengths and major problems can be identified. The advent of structured diagnostic interviews for adults, and now for children, has provided a major methodologic advance that increases the reliability of diagnosis. The use of structured diagnostic interviews to define diagnostic subtypes has also progressed.

In spite of the advance in structured interviews and operational definitions, however, several important diagnostic problems and disagreements persist. First, there are problems in the assessment of intermediate clinical states in children and adults who do not meet the DSM-III criteria for a particular category. Third, the evaluation of clinical characteristics such as chronicity, severity, and social function that extend beyond diagnosis is often viewed as essential to characterizing patients adequately.

And finally, the role of personality disorder in vulnerability may be crucial so that the assessment of such disorder might need to be part of any diagnostic evaluation.

Another problem in assessment for vulnerability research has been the importance of identifying early signs of disorders to be studied. There is little information to date on early specific signs of schizophrenia or depression before the onset of clinical syndromes themselves. In fact, any such focus on the evolution of states before illness onset is made even more difficult by the discontinuities in development displayed by both children and adults. These discontinuities occur in psychological, biological, and behavioral realms.

For example, any given trait, such as "aggression," may be reflected in different behaviors over time. Thus, too concrete an approach to pre-illness assessment might actually miss some of the continuities and discontinuities involved. To deal with these issues more effectively, it will be essential to have developmental psychologists become more involved in studying psychopathology and its developmental aspects than has been customary.

These multifaceted diagnostic needs for vulnerability studies highlight the difficulties encountered when attempting clinical assessment for vulnerability research. These difficulties are compounded in those projects evaluating young children, and in all studies using a single assessment method. Even the duration of the evaluation procedures is important. Experience suggests, for example, that some subjects provide additional crucial diagnostic information as they get to know the investigator over time.

Statistical Analysis and Project Design

Vulnerability research poses many complex issues of design and statistical analysis. Several areas were highlighted at the conference. Even the selection of a group at risk is more complex than it has sometimes appeared. The most common practice is to identify persons as vulnerable because they have a parent with the disorder. But most persons developing schizophrenia, for example, do not have parents with schizophrenia. For such reasons, it is particularly important to develop alternative means other than parent diagnosis for identifying subjects at risk.

One crucial issue in project design for vulnerability research is the choice of comparison groups. Naturally, selection depends on project goals as well as subject availability, but certain general principles also hold. The experience with studies of vulnerability to schizophrenia suggests that a comparison group of persons without psychiatric disorder is important, but a comparison group of other kinds of functional psychoses, or at least another group of patients with psychiatric disorder is also crucial. These two kinds of comparison groups permit identification of variables that deviate from norms and those thought to have been indicators of risk for a particular disorder that turn out to be
indicators of risk for psychiatric problems in general.

The paucity of behavioral differences between persons vulnerable to affective psychoses and those vulnerable to schizophrenia has raised many issues relevant to project conceptualization and design. Are these two groups so similar because the behavioral antecedents of the two major disorders are, in fact, indistinguishable? Or, in the studies where vulnerability is defined by being an offspring of a parent with psychiatric disorder, are they similar because both risk groups share in common the experience of living with a psychiatrically disturbed parent? At a time when it becomes possible, one way to resolve this dilemma would be to collect prospective data on children at high risk for both psychoses (e.g., on the basis of psychophysiologic abnormalities) who do not have a parent with psychiatric disorder. The problem with this approach is the uncertainty about the specificity of biological or psychologic risk factors.

Assessing the evolution of vulnerability poses other types of design problems. One challenge occurs when a vulnerable subject is assessed and receives multiple diagnoses. Establishing a diagnostic hierarchy is one way of resolving the problem of identifying patients for certain groups. However, the DSM-III criterion for hierarchy of diagnosis, the disorder for which the patient came to treatment, may designate the most transitory of the disorders the patient has and thus may not be very useful for vulnerability research. As an alternative to the DSM-III hierarchy rules, other principles, such as those of Foulds, that describe a hierarchy from personality disorder to psychoses might be considered.

Analogous hierarchies may be needed to help resolve a number of questions arising from a longitudinal focus on the identification of a particular outcome of the presumed vulnerable subject. For example, is a child who becomes schizophrenic and then recovers a schizophrenic outcome? At least tentative answers to such questions based on explicit theoretical or methodologic concern are essential in these projects.

In collecting outcome data, other issues arise as well. How narrow should the range of inquiry be? Should competence and health be asked about as well as illness and dysfunction? Is a good outcome as important to identify as illness? Logistically and humanistically, it is important to note that many subjects at followup interviews want to show how well they are doing and resent investigators focusing totally on defects.

Several statistical issues are raised by the study of vulnerability. Since this type of research often involves complex causal models, multivariate statistical approaches are frequently needed but may be used in ways that are not optimal or even appropriate. In some instances, for example, the distribution patterns of the data selected often do not meet the basic assumptions of the statistical procedures employed. To some extent, this and related problems with the use of multivariate techniques may be at least checked by employing several methods of data analysis to construct a "multi-method" context for studying complex data.

Other statistical problems posed by missing values, or by unrecognized subgroups in a population, are also common. Data collection and analysis procedures used in longitudinal vulnerability studies often tend to employ methods derived primarily from cross-sectional research and do not deal with the unique potentialities and demands of longitudinal data. Advances in time series analysis and in considering state change provide two unique ways for analyzing data in a truly longitudinal fashion.

But it is possible to go even further. One of the major issues in longitudinal analysis is the focus of developing strategies for understanding the evolution of disorder and its etiologies in contrast to more static approaches for measuring merely the existence or amount of change from one time to another. Although the exact dividing line between these two goals is somewhat arbitrary, the analyses and definition of variables required for understanding the evolution of a process and its dynamics can involve quite different approaches from those for noting change between cross-sectional points. Both approaches, naturally, can be considered along several dimensions if the data and concepts so warrant.

If one focuses on processes driving the etiologies and evolution of disorder, many concepts from statistics and physics can be applied in interesting ways. These concepts include such notions as: (1) what force is required to make changes; (2) the sources of resistance to changing states; and (3) the subject's rate of change or sojourn in a particular state. All these concepts generate particular approaches to choosing what variables should be assessed, when they are assessed, and how to analyze the data obtained.

One final point related to data analysis in the vulnerability approach to studying etiology should be made. It is important to recognize that we are attempting to account for human heterogeneity. Although certain efforts toward identifying mass commonalities may be valuable,
those who have carried out research on vulnerability have generally been greatly impressed by how tenuous many such mass categorizations appear.

**Family and Personality Variables**

**Family Variables.** Techniques for assessing families have developed greatly in recent years. Observation, interview, and self-report measures are available and can be useful in evaluating families for the purposes of vulnerability research. But any one of these approaches may be inadequate in itself, depending on what is to be assessed. Often two or even three will be required.

Just as there are various approaches to family assessment, there are different models for considering family impact. Although the genetic model has been most popular recently, the cognitive social-learning model is becoming recognized increasingly as also important. The social learning model suggests, for example, that parental impact can be studied by viewing parents as teachers and noting strengths or problems in their teaching efforts.

Whatever the content focus, there has been some tendency in family studies to investigate general parental traits rather than dynamic interactions between parents and their offspring. It will be important to explore more specifically those interactions that may be most crucial to child development, namely the rearing behavior of parents.

The assessment of family characteristics and the consideration of developmental factors in potentially vulnerable offspring are closely intertwined. Although in studies of children most vulnerability studies have focused on the development of cognitive functioning, further attention to affective functioning and its development is also needed.

**Personality Characteristics.** Personality factors as they relate to vulnerability for psychiatric disorder are extremely complex. This has implications both for their assessment and for understanding their role in vulnerability. A particularly helpful way of categorizing personality impacts is to consider them as: (1) etiologic precursors of a disorder, (2) early forms of a disorder, (3) influencing the quality of a disorder, and (4) generated by the disorder. Such distinctions are a minimum requirement for introducing the study of personality characteristics into vulnerability research.

Although personality factors are difficult enough to assess in adults, their evaluation in children is even more complicated. Identifying important traits and clarifying at what age these traits might become present or disappear is essential. A review of the literature in this area would be extremely helpful.

**Biochemical and Physiological Markers**

A range of biological characteristics (e.g., attention, neuromotor function, arousal, and familial-genetic factors) all show promise in vulnerability research. However, findings are still controversial, with neither the clinical assessment nor the biological measures currently advanced enough to provide definitive results. Conceptually, it is important in looking for biological markers to measure state as well as trait characteristics. This is particularly important with autonomic functioning or other characteristics that may be influenced by a particular phase of the disorder or by medication the patient is receiving.

Even the biological characteristics that are results of genetic inheritance can change over time, complicating the study of biological markers still further.

Increased clarification of homogeneous clinical entities (for example, the distinction of unipolar, endogenous, and delusional depression) may hold major keys to successful biological studies in understanding vulnerability processes. It will also be valuable to employ more fully the existing etiological theories for depression and schizophrenia (such as childhood loss, mother-child bonding, dependent schizoid personality, learned helplessness, and vulnerability beyond a narrow range of stimulus) to focus the collection and analysis of biological data still further. Pending future advances in biological studies of vulnerability, it may be helpful to keep a list of those large high-density families who have a particular disorder.

**Comparing the Vulnerability to Schizophrenia and Depression: Models of Causation and Possibilities for Collaborative Research**

Can the investigators of vulnerability to depression and those studying vulnerability to schizophrenia collaborate in useful ways? The conferences decided the possibilities were limited at this point. To some extent, the disorders have differences that make immediate comparison and collaboration difficult. Depression has all gradations of severity, including a depressive personality type. In schizophrenia, the existence of such gradations is highly controversial. Another source of difference comes from relative stages of knowledge in the two content areas. Vulnerability to depression in the offspring of parents with depression is just
Many investigators studying children at risk for depression are using case-control designs with specific diagnoses as the major dependent variable in children (e.g., depression, attention deficits). This contrasts with the range of nondiagnostic variables used in studying the children of schizophrenic parents. The predominant diagnostic focus in the study of depression is possible in part because there is increasing evidence that major depression can be diagnosed in children. This contrasts with schizophrenia, which is rarely diagnosable before mid-adolescence.

The model used in the depression high-risk studies is often an epidemiologic approach in which multiple risk factors from a variety of domains (biologic, psychosocial, and genetic) are included. The relatively high prevalence of affective disorders as contrasted with schizophrenia makes such studies particularly promising.

Although the differences between studying vulnerability to depression and schizophrenia are important, it seems possible that these differences might be used to produce cross-fertilization rather than isolation of the two research efforts. For example, the clear definition of risk in epidemiological terms that has been used in studying vulnerability to depression is something which many of those studying vulnerability to schizophrenia could employ more effectively. The concept of risk, in contrast to the concept of vulnerability, which is more general, provides a body of statistical approaches for research and a way of relating to epidemiological fields in mental health. In contrast, those studying vulnerability to schizophrenia tend to focus efforts on problems of: (1) complex interacting systems, (2) a variety of outcomes, (3) general as well as specific risk factors, and (4) the potential role of protective factors. These considerations might be incorporated more effectively into research on vulnerability to depression as well.

Both groups of investigators may need to consider more seriously the reasons that some concerns are not shared with the other group. In fact, there may be many potential commonalities that are being missed. Both groups, for example, need models for studying the particular disorder in which they are interested, which may well include models for understanding the etiology of psychiatric disorders generally. The translation of such models into empirical research procedures is crucial for both groups.

Some collaboration between the two areas of study has already begun in the sharing of methods between research groups. A joint article about optimal research design for studying vulnerability would be an especially valuable way for identifying some of the common issues as well as developing the field more generally. Such a report might also describe which methods of data collection and analysis are valuable, what new ones are needed, and what conceptual models can best serve the field.

Further Recommendations From the Conference

Several recommendations were generated during the conference by these considerations. It was recognized that in the future a broader range of groups studying vulnerability should be included in any joint meetings growing out of this conference. In any future meeting, introductory statements regarding the history and key issues in the two groups as clarified in this conference would be important. Specific projects might be discussed in greater depth as examples.

A critical review of the literature is needed to cover available methodology for the assessment of personality structure and functioning at various stages of childhood development. The aim of such an effort would be to provide a state-of-the-art review in order to stimulate new research on two fronts: (1) the development of personality measures appropriate for children and adolescents, and (2) the carrying out of prospective studies on personality development. These are basic developmental research activities that are badly needed in their own right, but are particularly important because of their relevance to clinical research on developmental psychopathology.

There is a need for reliable and valid assessment instruments and associated normative data regarding the different human emotions at different ages and stages of maturation. Except for sporadic efforts, there is little research that focuses on the development of various emotions, their biological and behavioral bases, and their modes of expression.

A very impressive feature of the conference was the diversity of disciplines and of the areas of clinical research represented by the participants. A corollary and equally impressive feature was diversity of terminologies used, often with a wide range of different meanings. A glossary may be required to overcome the resulting problems. At the very least, investigators will need
to specify the meaning of key terms they use.

Reference
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