nonunitary disease hypotheses

A review of the literature and research on the biochemical and genetic theories of schizophrenia reveals a startlingly simple, yet potentially significant error in epidemiological investigation. Most of the research designs assume a unitary disease hypothesis for schizophrenia in spite of a multiplicity of theories to the contrary. While many investigators are certainly aware of nonunitary hypotheses, their research reflects a search for a single cause or a single cure for schizophrenia. In the Comprehensive Textbook of Psychiatry Herbert Weiner (1975) warns: "If one assumes that schizophrenia is not a unitary disease with a stable course and that any group of schizophrenic patients probably represents a heterogeneous population, it may be necessary to compare not only mean values of the experimental and control data but also the deviance in individual and mean values in each group" (pp. 882-883). Clearly, we must design a sampling technique or research methodology that will enable us to test a nonunitary hypothesis.

There is much support in the psychiatric research literature for the concept that schizophrenia is a syndrome rather than a solitary disease. There is evidence for a multifactorial genetic pattern of inheritance, limited phenotypic penetrance, and an etiology of multiple and possibly interacting factors: physiological, genetic, social, experiential, and psychological. If these theories are correct, then there is the danger of rejecting a valid cause or a specific cure under an incorrect unitary null hypothesis. Many other errors in technique and sampling have resulted in the refutation of previous studies conducted under the assumption of a unitary etiology of schizophrenia. These other errors have preempted more fundamental challenges of underlying hypotheses. Had these methodological deficits not been recognized, potential etiologies and remedies might have been "correctly" rejected in the search for a panacea and a single cause for a syndrome with multiple etiologies and efficacious specific cures. Had the same assumptions and methodology been applied to the investigation of fevers, the tubercle bacillus might have been rejected as a cause and penicillin as a cure for fever.

In the modern era of genetics and neurochemistry there is no useful system of phenomenologically categorizing the majority of schizophrenias which distinguishes them by etiology or response to specific therapy. The neo-Kraepelinian nosology of the DSM does not make distinctions that have been useful in predicting responses to medication or defining subpopulations for testing etiologic hypotheses. The older dichotomy of process and reactive schizophrenia has so far also been fruitless. Schizophrenic symptoms are all nonspecifically ameliorated by the same "common-pathway" antipsychotics, perhaps analogous to a fever's response to salicylates, regardless of etiology.

In this century, however, careful observation and history taking helped to distinguish several forms of "schizophrenia" and led to an understanding of their etiology and ultimately to their cure. Toxic deliria, general paresis, pellagra, and amphetamine psychosis are all forms of dementia praecox which have been distinguished from idiopathic schizophrenia. A reexamination of the phenomenology of schizophrenia, coupled with a search for previously unknown associated signs and symptoms, may be necessary if we are to uncover the etiologies and multifactorial pathophysiology of the syndrome of schizophrenia.

How can we improve our research techniques to include a nonunitary hypothesis? Can we reevaluate some of the research of the past with such a hypothesis and learn something new? How can we better sample the population of schizophrenics, and how can we more accurately control our investigations? The examples of fever, hypertension, and mental retardation suggest models for future research.

Reference


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