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Using Clinical Data Bases to Study Schizophrenia

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Studying psycho-pathology using clinical registries enables a birds-eye view of all mental illness, and allows researchers to look at each illness in the context of other mental illnesses. The papers presented in this issue indicate that at least some of the symptoms commonly present in schizophrenia are actually present in other mental disorders and may even be present in individuals without diagnosed psychiatric disorders. Although there are some disadvantages to research based on clinical registries, this method enables study designs not be possible with conventional research paradigms.

Key words: mental illness/schizophrenia/clinical registries

Introduction

For pragmatic and scientific reasons, most researchers study a specific illness. They identify patients who meet diagnostic criteria, find matched controls, and test/measure their target of interest. Studying illness using clinical registries enables a birds-eye view of all mental illness and allows one to look at each illness not only to itself but also in relation to other mental illnesses. This is particularly relevant in psychiatry where the mere concept of illness, the boundaries separating between different illnesses, the syndrome status of many diagnostic classes, and the boundaries separating between illness and variants of normal behavior are a moving target. This special issue of *Schizophrenia Bulletin* on clinical registries utilizes this approach.

Psychiatric Illness as a Continuum

The paper by David et al, addresses the issue of cognitive impairment, a domain of impairment considered a core pathology in schizophrenia. The data, taken from a cross-section of recruits to the Swedish military, show that cognitive impairment is present in all diagnostic groups of mental illnesses and is not restricted to schizophrenia. This in turn indicates that schizophrenia might be conceptualized as lying on a continuum of psychiatric illnesses which have in common cognitive impairment, with schizophrenia, perhaps, being on the more severe end of the spectrum.

Paternal age

Over the past 8–9 years, a plethora of articles have reported that advanced paternal age is a risk factor for schizophrenia. Poor social abilities are also a ''hallmark'' of schizophrenia and are considered an intermediate phenotype of the illness. The article by Weiser et al addresses the relationship between advanced paternal age and social functioning in persons without mental illness. The article reports a small but significant association between advanced paternal age and poorer social functioning in the general population. This indicates that part of the risk for schizophrenia inferred by advanced paternal age might be mediated, at least partially, via the effect of advanced paternal age on social functioning. Here again, this ''view from above'' reveals interactions which would have been missed in study designs which compare cases of schizophrenia with controls. These findings are also significant regarding future research, indicating that the study of the causes and treatment of cognitive and social dysfunction is relevant to all areas of psychopathology, not only to schizophrenia.

Genetics

So it seems that that at least some of the symptoms commonly present in schizophrenia are actually present in other disorders and, indeed, are present in individuals without diagnosed psychiatric disorders. The next step might be to study the genetic underpinnings of these phenomena, by studying the genetics of specific symptoms, and not of clinical syndromes. An example of this approach is utilized by DeRosse et al who examined the association between genotype and individual symptoms of schizophrenia. They found significant genetic risk factors for both reality distortion and disorganized symptoms.

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Famine

The article by Brown et al used clinical registries to examine the effects of nutritional deficiencies in utero caused by famine and confirmed an increased risk for schizophrenia in the off-springs. This illustrates the power of discovery based on clinical registries that would not be possible with conventional research designs.

Disadvantages

There are definite disadvantages to research based on clinical registries. The design is predetermined and cannot be manipulated. The large sample sizes encourage "fishing expeditions," which often yield statistically significant findings, but have no real meaning, and might even be misleading. The assessments are clinical and are usually not done using validated research instruments. Also, the data suggest pathophysiological mechanisms but is never useful in elucidating mechanism. On the other hand, if one looks at the research findings in the field over the years, it is mainly the epidemiological findings that have been replicated, whereas many of the more "biological" findings often do not replicate. Most importantly, this approach does not address the most important question which the field has yet to solve, namely: what distinguishes the ill brain from the healthy brain.

Conclusion

It is probably most appropriate to conclude that, in the absence of definitive neuropathology, clinical registries are vital in providing decisive leads on etiology and insight on psychopathology. The example of using registries to understand cardiovascular risks (cholesterol, hypertension, life style) has been the impetus to study and understand cardiovascular pathophysiology and ultimately devise effective therapies. Research using clinical registries provides direction toward the ultimate understanding of the biology of behavior and of mental illness.