Introduction

Mental Disorders in the Genomics Era

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The Genomics Era in medicine began in early 2001 with the publication of a draft of the human genome sequence. We use the label “Genomics Era” since, for the first time, we have a complete roadmap of our entire genome. This roadmap is helping to guide us toward new approaches to the diagnosis and treatment of a host of disorders ranging from Alzheimer’s disease to deafness. The finished sequence is still years away and the complete annotation of all functionally relevant stretches of the DNA sequence will take even longer. But we are already beginning to ask the questions: how will the study of psychiatric diseases progress in the Genomics Era? How can we begin to address the complex ways in which genes interact with environment to produce mental illness? When will the fruits of genomic research affect the diagnosis and treatment of mental illnesses such as bipolar disorder? In this month’s issue of CNS Spectrums, we have assembled a group of papers aimed at addressing these questions.

In the first article, Lange and McInnis review the controversial issue of anticipation in mental illness. Many psychiatric illnesses display the drop in age at onset and an increase in severity of illness across successive generations that are the key features of anticipation. At least eight modern studies in bipolar disorder alone, have addressed the issue of anticipation, and all eight conclude that a significant decrease in age at onset, a significant increase in illness severity (usually measured as frequency of manic and depressive episodes), or both occurs within families containing multiple cases of bipolar disorder. The key question is not whether anticipation occurs, but what it means. Is the observed anticipation merely an artifact of subtle ascertainment biases? We now know that anticipation is not always an illusion, but sometimes reflects an interplay of heritable and environmental factors to produce mental illness. This has been enriched in recent years by the addition of novel methods of genetic investigation and the core methods of family, twin, linkage, and association studies. Anticipation in psychiatric illness remains a conundrum in psychiatry that genetic findings may soon help to solve.

The core methods of family, twin, linkage, and association studies are increasingly complemented by novel methods based on new concepts of dynamic mutation, epigenetics, and functional genomics. One of my introductory questions (When will the fruits of genomic research affect the diagnosis and treatment of mental illnesses?) must remain unanswered for now. The fruits of the Genomics Era do not necessarily produce the most promising results. This month’s articles help light the way, even though the destination is uncertain.

In the future, genetic findings may form the basis for many new treatments in psychiatry. For now, we are forced to make the most of the existing pharmacologic armamentarium. This has been enriched in recent years by the addition of antipsychotics and novel anticonvulsants. Finally, Kahn and Chaplan review mood stabilizers currently in use or soon to be released for general use, asking whether any are “good enough” for the task of preventing and treating episodes of mania and depression over time. They conclude that no single ideal mood stabilizer exists, but that the skillful and judicious use of multiple complementary medications often yields the best results. This conclusion highlights a conundrum in psychiatry that genetic findings may ultimately allow us to move beyond: why should several medications with radically different apparent modes of action all possess mood stabilizing properties?