Molecular Genetics: Progress and Potential
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This is the second and final issue of this series in which we explore the progress and potential of the field of psychiatric genetics. Some of the studies highlighted represent new conceptual frameworks for studying genetic transmission. These frameworks include sensitivity to infection, variable drug response, and neurodevelopment as techniques for defining more specific phenotypes, and ultimately genotypes, within a particular diagnostic category.

Pato et al begin this issue with a review of the current state of knowledge in the genetics of bipolar disorders. Historically, the work in bipolar disorder is significant because it bridges both the optimism of early positive findings and the subsequent cynicism and disappointment when these early positive findings did not hold up. They also present new reason for optimism in understanding the genetics of bipolar disorder based on strategies for both population selection and laboratory exploration. The work by Ozdemir et al focuses on an exciting new strategy for defining phenotype based on drug response—in this case, response to clozapine treatment for schizophrenia. This work pulls together not only the drug response but the pharmacokinetics of drug metabolism of the individual patient. Ultimately, genetic explorations such as this could provide information that would allow every clinician to provide the optimal treatment strategy for each patient.

Genetic research in anxiety disorders, such as obsessive-compulsive disorder (OCD) and panic disorder, is just beginning, and the papers by Pauls and Marazitti and Rotondo review the classic findings from twin studies. These findings make a compelling argument for a genetic component for these disorders. In addition, the Pauls paper stresses the importance of defining phenotype carefully in the further exploration of the genetics of OCD. The Marazitti and Rotondo paper reviews the initial work in linkage analysis and associations studies in panic disorder, which has been inconclusive to date. The final two papers in this issue present two exciting and innovative ways of exploring genetic factors in psychiatric disorders. The Rapaport and McAllister paper reviews work on an autoimmune mechanism for some cases of OCD. This may represent a very specific phenotype of the disorder with inheritable vulnerability. This paper also highlights the potential power of exploring very specific phenotypes of a more broadly defined disorder. Finally, the Muglia et al paper takes a hypothesis driven approach to guide the exploration of potential genetic factors. They propose lines of evidence indicating potential neurodevelopmental defects in patients with schizophrenia. Therefore, they suppose it might be valuable to look at polymorphisms among genes that control neurodevelopment in patients with schizophrenia. Not only do they review preliminary work for a number of neurodevelopmental loci, but they also present an important line of thought that could be used in the study of other psychiatric illnesses.

These two issues attempt to present new findings as well as review existing data on a broad spectrum of psychiatric disorders including schizophrenia, bipolar disorder, OCD, attention-deficit/hyperactivity disorder, substance abuse disorders, and panic disorder. More importantly, they have tried to present the strategies and new directions being used in this field to tease out the genetics of these complex disorders.

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