Preface

Over the past decade, the methods available to analyze the genetic basis of behavioral phenotypes have changed enormously. Early enthusiasm about the role that genetics would play in our understanding of mental disorders was tempered in the late 1980s by the failure to replicate a number of well-publicized claims of linkage for bipolar affective disorder and schizophrenia. It is now well recognized that the gene-hunt battle will be long and difficult. Discrepant results have stimulated the development of the genetic epidemiological and statistical strategies used to study complex genetic disorders, and have led to refinements in phenotype analyses.

Our objective in *Psychiatric Genetics: Methods and Reviews* is to provide a comprehensive overview of the tools and methods that are currently available in psychiatric genetics, as well as archetypical examples obtained using these strategies. In particular, Part II of this book tackles the following methodological issues: study design, molecular techniques, clinical interviews, and population sampling methods. Part III of this book focuses on alternative methods for characterizing phenotypes with the aim of identifying entities with better genetic validity.

In the first chapter of Part II, Elena Grigorenko and David Pauls point out the advantages and limits of each study design for genetic epidemiology. They offer a clear vision of some much-debated problems, such as the power of detection, sensitivity, and specificity of each of the methods. Thomas Bourgeron and Bruno Giros provide an overview of the classical and novel gene-identification strategies available for the study of complex diseases. The future development of relevant molecular techniques is also usefully described.

Philip Gorwood gives a comprehensive review of the available clinical interviews for the assessment of classical nosographical entities. This chapter should enable psychiatrists to choose the most relevant clinical instrument for a particular research purpose. Sampling procedures for patients, subjects at risk, and controls are critical issues for the analysis of genetic vulnerability and protective factors implicated in psychiatric disorders. The advantages and limits of these sampling procedures, as well as potential sources of bias, are considered in the chapter written by Frank Bellivier.

The third part of *Psychiatric Genetics: Methods and Reviews* is introduced by Marion Leboyer in a comprehensive review of new phenotypic strategies, i.e., candidate symptoms and endophenotypes, and their scientific rationale. Although
research in this field started only recently in psychiatry, the applications of these strategies have already provided exciting results. The results of the leading groups in cognition, brain imaging, and biochemical endophenotypes are summarized in this section. Michael Egan and Terry Goldberg give a brilliant and comprehensive review of their own work and the literature on cognitive intermediate phenotypes in schizophrenia. They provide the first evidence of an association between a cognitive deficit and a genetic polymorphism. This result suggests that there are links between genes and behavioral phenotypes.

A review of the biochemical endophenotypes observed in personality disorders is then presented by Antonia New and Larry Siever. They hypothesize that personality disorders may form biologically mediated traits that predispose individuals to the full-blown disorders.

Robert Freedman, the leading figure in the field of physiological endophenotypes, then describes the data obtained in genetic analysis of eye-tracking dysfunction, P50 and P300 as endophenotypes in schizophrenia and alcoholism.

Joseph Callicott and Daniel Weinberger provide a thorough review of one of the most promising approaches for the identification of valid phenotypes, i.e., the union of neuropsychological experimental designs and in vivo physiological brain mapping.

In the concluding part of this book, Ming Tsuang, Levi Taylor, and Stephen Faraone give a brilliant perspective on the methodological and ethical challenges that psychiatric genetics will face in the future.

*Psychiatric Genetics: Methods and Reviews* tells the very beginning story of a complicated, yet promising, saga in the field of psychiatric genetics. The message is clear: it will not be possible to unravel the complexities of psychiatric genetics unless we can precisely identify the phenotypes involved.

*Marion Leboyer, MD, PhD*

*Frank Bellivier, MD, PhD*
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