

Genetic Influences on Response to Drug Treatment for Major Psychiatric Disorders

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Editors

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Introduction

Psychiatric disorders affect a significant percentage of the population, making the issue of their optimal treatment an extremely important one. A judicious use of pharmacological treatment would be the most appropriate and effective method of help to most of such patients. Interindividual genetic variations can influence the responses of patients to any psychotropic medications; therefore, the results of studies investigating genetic background of such a mechanism could facilitate the effectiveness of the treatment.

Pharmacogenetics of the treatment of psychiatric disorders has become a rapidly expanding area in the last two decades. This has been mostly caused by the introduction of molecular genetic methods to the field. The most used approach for pharmacogenetic studies of efficacy and safety of treatment with individual drugs is still a “candidate gene” method. However, recently, genome-wide association studies (GWAS) have also been entering into this subject, exemplified in this book by the GWAS of lithium response in bipolar disorder. Due to the progress in molecular genetics employed for estimating psychotropic drug response, “pharmacogenetics”, which assesses genetically determined interindividual differences in response to drugs, has been gradually becoming “pharmacogenomics”, which uses genome-based technologies for this purpose.

The issue of pharmacogenetics (pharmacogenomics) of psychiatric disorders has been recently covered by several books, the most important ones published in 2010–2011. The first book to mention is *Psychiatric Pharmacogenomics*, published in 2010 and authored by the late David Mrazek (1948–2013). The idea of the book is an original one, showing a contribution of 14 genes (four cytochrome genes, three neurotransmitter transporter genes, three serotonin receptor genes, and three dopamine receptor genes) to response of psychotropic drugs in various psychiatric diseases. Another book, published in 2010, came within the Karger series of *Advances in Biological Psychiatry*, titled *Pharmacogenomics in Psychiatry*, and edited by Matthias Schwab, Wolfgang Kaschka, and Eduardo Spina. In this book, the pharmacogenomic findings in individual psychiatric conditions, such as schizophrenia, depression, attention-deficit/hyperactivity disorder, eating disorders, and personality disorders, have been reviewed. And finally, in 2011, the last edition of

Bernard Lerer's book, *Pharmacogenetics of Psychotropic Drugs*, which was first published in 2002, was released. This is the most comprehensive publication, covering both the clinical and molecular background of this topic, as well as pharmacogenetics of specific psychotropic drugs and disorders.

Several years have passed since the publication of these books, and the aim of this one is to cover the major developments in pharmacogenetics and pharmacogenomics of major psychoses in the last two decades, including also the period 2010–2015. However, the book we are presenting here is unique in several aspects compared with the books mentioned previously. Written by global experts, this book provides a modern comprehensive insight into the pharmacogenetics of treatment of major psychoses: schizophrenia, bipolar disorder, and depression. Secondly, the pharmacogenomics of three categories of the most important psychiatric drugs such as antipsychotics, antidepressants, and mood stabilizers has been updated and reviewed. From the point of view of mainstream psychiatry, both these diagnostic and drug categories have made the most significant topics in recent years.

The main practical aim of pharmacogenetics and pharmacogenomics of psychotropic drugs is to make drug treatments in psychiatric medicine more effective in individual patients. Therefore, a related issue to pharmacogenetics in psychiatry is that of personalized medicine. This model proposes that each medical intervention (e.g., pharmacotherapy) should be tailored to the individual patient. The term personalized medicine was first coined in the context of genetics; thus, the use of genetic information about pharmacotherapy (i.e., pharmacogenetics) makes the most important contribution to this field. Although this model has still not been widely used in psychiatry, the amount of pharmacogenetic data presented in this book may greatly contribute to reaching clinical practice by personalized prescription in the not so distant future. There is a significant role of modern psychiatric pharmacogenetics to meet such expectations.

Apart from providing a timely overview of what has been achieved in the area of psychiatric pharmacogenomics in the last two decades, this book also mentions some promising directions and perspectives for future research. The first direction is connected with the development of molecular genetics. The GWAS study of lithium response in bipolar disorder has been already performed, and such research with other drugs used in major psychoses could be possible in the future. Other developments in this field such as microarray technologies and sequencing techniques may be shortly available for the pharmacogenomics of psychotropic drugs. Also, the studies of epigenetic mechanisms such as DNA methylation, histone modification, and regulation by miRNA have been gradually introduced in pharmacogenetic research. Another area of research is linking pharmacogenetic assessment with biomarkers, including neuroimaging ones. Studies exemplifying such approach in depression were reviewed in a chapter of this book.

Finally, the attempts to use pharmacogenetics of antipsychotic, antidepressant, and mood-stabilizing drugs in practice are presented in the last chapter of the book. The clinical utility of pharmacogenomic testing has been evolving; although, at a slower pace than it has been anticipated. We are just on the threshold of introducing new pharmacogenetic tools for psychiatric practice, and one of such test (GeneSight)

is now reimbursed by Medicare in the USA. It may be expected that several other tools of this kind will enter psychiatric practice in the next years.

We sincerely hope that reading this book, many physicians (mostly psychiatrists) and pharmacologists, as well as all those engaged in clinical and experimental neuroscience, will find it useful; not only as an update to present art of knowledge in pharmacogenetics of drugs used in major psychoses but also for providing new insights into the development and applications of pharmacogenomics in psychiatry.

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