Preface

Psychiatrists have followed developments in the rapidly expanding field of pharmacogenetics and pharmacogenomics with great interest. Methods for making drug treatment more effective have been the central focus in psychiatric medicine in recent years ('the right drug for the right patient'). However, improvements in drug efficacy and tolerability and finding of the optimal dosage can only be realized if in vivo mechanisms of drug action (pharmacodynamics) and ADME (absorption, distribution, metabolism, excretion) processes (pharmacokinetics) of psychopharmacological agents are better understood. The urgent need for further progress in this field is obvious.

A number of comprehensive multicenter studies have shown that, in terms of efficacy and tolerability, the pharmacological treatment strategies presently available for common psychiatric diseases are still far from satisfactory. For example, in the first level of the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial, only about 30% of patients were in remission after follow-up of 12 weeks' drug therapy using a selective serotonin reuptake inhibitor [1]. There is also a substantial body of evidence available indicating that even amongst antidepressant responders residual symptoms are common and associated with poorer psychosocial functioning as well as increased relapse rates [2]. As far as schizophrenia is concerned, pharmacological treatments which block the dopamine system are usually effective for delusions and hallucinations, but less so for disabling cognitive and motivational impairments [3, 4]. The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study showed, among other things, that non-compliance to prescribed medication is a major clinical problem in antipsychotic therapy. For instance, Lieberman et al. [5] reported that the majority of patients in each of several study groups receiving different antipsychotics discontinued their assigned treatment owing to inefficacy or intolerable side effects or for other reasons.

In this volume of *Advances in Biological Psychiatry*, current progress and perspectives in pharmacogenetic testing of drug-metabolizing enzymes, drug transporters and other drug targets involved in the response to psychotropic agents are described extensively. There are great expectations that in the near future pharmacogenomics will provide us with the means of identifying subgroups of patients which are at risk of therapeutic failure or more vulnerable to certain adverse effects of psychopharmacological agents. To mention just two examples from recent years: an association has been detected between treatment-emergent suicidal ideation in individuals receiving citalopram therapy and polymorphisms near the cyclic adenosine monophosphate response element binding protein (CREB-1) gene [6]. In another example, data from a study conducted by Opgen-Rhein and Dettling [7] suggest that certain groups of patients carry a genetically determined proneness to clozapine-induced agranulocytosis (as described in this volume by Buckley et al.). Of course, these findings have to be replicated and further research will be necessary in these areas.

Although polymorphisms of genes are useful markers to explain interindividual variability in ADME processes and drug response, the early enthusiasm about the promise of individualized therapy in psychiatric diseases and personalized medicine in general has been tempered by the complexity and multifactorial character of drug responses [8]. Impressive developments in a number of genomic profiling approaches – such as microarray technologies, genome-wide association studies and most recently the next-generation sequencing technique – have given rise to the hope that more comprehensive information about a patient's genomic profile will be available in the near future for improvements in patient care in psychiatric medicine. Moreover, epigenetic mechanisms (i.e. DNA methylation, histone modification and regulation by miRNA), which may result in individual modification of gene expression and phenotype without affecting the DNA sequence, need to be considered as important players in the complex interactions between the multiple genes and environmental factors shaping a distinct phenotype.

This volume presents a timely overview of what has been achieved up to now in the field of psychiatric pharmacogenomics and some promising directions and perspectives for future research that could ultimately lead to substantial improvements in treatment.

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