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Introduction

Neuropsychiatric disorders represent the second largest cause of morbidity and premature mortality worldwide. The World Health Organization has estimated that, collectively, neuropsychiatric disorders comprise 13% of all reported diseases. These disorders include major depression, anxiety, schizophrenia, bipolar disorder, obsessive-compulsive disorder, alcohol and substance abuse, and attention-deficit hyperactivity disorder and account for 50% of the disability in less developed and developing countries.¹ Approximately one in five Americans will experience an episode of a psychiatric illness such as schizophrenia, a mood disorder (depression and bipolar disorder) or anxiety in any given year.² The prevalence of these disorders, and their personal and societal costs, has fueled a half century of research aimed at elucidating the etiologies and pathophysiological mechanisms of these devastating disorders with the ultimate goal of designing pharmacotherapies that can correct the underlying neurochemical defects.

Many drugs in use today for treating neuropsychiatric disorders are refinements of compounds identified over 40 years ago and found to be effective by highly empirical and serendipitous observations. As the biochemical mechanisms

of action of the effective agents were elucidated, theories were put forward concerning the neurochemical bases for the disorders. Thus, in the 1960s, the dopamine hypothesis of schizophrenia and the monoamine theory of depression were introduced, based in large part upon the abilities of antischizophrenic drugs to block dopamine receptors and antidepressant drugs to increase synaptic levels of monoamine neurotransmitters. These concepts have continued to guide drug development efforts to this day. More recent research, particularly the identification of gene polymorphisms influencing a multitude of biochemical pathways, has revealed a molecular complexity of these disorders that was unappreciated until the past decade. It is increasingly clear that neuropsychiatric disorders arise from interactions of multiple predisposing genes of variable penetrance overlaid by diverse experiential and environmental influences.

The following review highlights the currently available research tools for the study of the five most prevalent neuropsychiatric disorders: schizophrenia, major depression, bipolar disorder, anxiety and attention-deficit hyperactivity disorder.