

PREFACE

The primary goals of schizophrenia research are to understand the causes of the disorder and to attenuate its symptoms. Advances in diagnosis and treatment have produced significant progress toward these aims, but there are still many hurdles to clear before the biological, genetic, and environmental etiologies of the illness are understood fully. Similarly, much work is needed to alleviate the residual and positive symptoms associated with schizophrenia. One important consequence of our progress to date combines our understanding of the etiology of the disorder with our understanding of treatment options. There is a clear consensus that better outcomes are associated with earlier initiation of treatment.

In fact, if a list of “holy grails” could be identified in schizophrenia research, none would rank higher than the development of strategies aimed at preventing the onset of the disorder. Prevention itself, however, is a multidimensional concept, and our current distance from the grail depends on which dimension is the focus of attention. Although primary prevention remains further off on the horizon, early intervention for psychosis and the development of psychosis (i.e., the prodrome) are active areas of investigation. One of the most significant impediments to both early intervention and prevention research is that we do not yet know what the liability to schizophrenia looks like. We do not know who will develop the disorder and who will not. As a result, we do not know who should receive treatment before their clinical symptoms become overt. This becomes more evident as the distance from psychosis increases. Prodromal symptoms, which are a target of many current models of early intervention, are often nonspecific for schizophrenia. Problems that may precede prodromal symptoms, such as negative symptoms, are even less clearly points on a trajectory to psychosis, as are the absence of clinical symptoms or other abnormalities (e.g., neuropsychological, psychophysiological, or neurobiological deficits) in individuals with one or more risk factors for schizophrenic illness, such as those with a family history of the disorder, pregnancy, or obstetric complications.

Fortunately, the situation is improving. High-risk longitudinal studies and family studies now identify a range of likely clinical, biological, cognitive, and social problems in relatives of patients with schizophrenia that may represent liability/vulnerability factors. A recent reformulation of Paul Meehl’s concept of schizotaxia supports the view that one or more liability syndromes might be identified and validated. There is also growing attention to the nature and delineation of the prodrome. Because interest in the prevention of schizophrenia is high, and characterization of liability syndromes has the potential to move pre-

vention research forward, the time seems right for a volume on prevention in schizophrenia. *Early Clinical Intervention and Prevention of Schizophrenia* focuses on the status of prevention research within the broader context of our current knowledge of the causes and early treatments of schizophrenia, with the goal of determining how early we can intervene in schizophrenic illness. To accomplish this aim, we invited experts working in the field to contribute chapters in the framework of four major sections. We also emphasized our reformulation of schizotaxia to substantiate the notion that the liability to schizophrenia often manifests itself with meaningful clinical, neuropsychological, social, and neurobiological concomitants.

The first section reviews the origins of schizophrenia. In order to develop rational interventions, it is crucial to understand what causes the illness and how it develops. Thus, this section focuses on the genetic (Steve Faraone and colleagues), early environmental (Sarnoff Mednick and colleagues), and neurodevelopmental (Stefano Marenco and Daniel Weinberger) determinants of schizophrenia.

With this framework in mind, the second section characterizes current views of the vulnerability to schizophrenia. In particular, it explores the nature of the liability from several dimensions, including the prodrome (Jaak Rakfeldt and Thomas McGlashan) and our proposed pre-prodromal syndrome of schizotaxia (Steve Faraone and colleagues). More specific manifestations of schizotaxia—used here in a generic sense to describe the liability to schizophrenia—include cognitive deficits in high-risk populations (Allan Mirsky and Connie Duncan) and in adult, nonpsychotic, biological relatives of patients with schizophrenia (William Kremen and Anne Hoff), socioemotional deficits (Elaine Walker and Karen Hochman), neuroanatomical abnormalities (Larry Seidman and colleagues), and neurophysiological deficits (Marina Myles-Worsley). Finally, Robin Murray and colleagues review several of the dimensions considered in previous chapters to determine whether schizophrenia is actually predictable.

The most important value of characterizing the liability to develop schizophrenia involves, arguably, the identification of treatment/intervention targets. In this light, the third section addresses issues of early intervention and prevention more directly. Following a discussion of conceptual and methodological considerations necessary for the design and implementation of prevention protocols (Hendricks Brown and Steve Faraone), the focus turns to protocols for the treatment of schizotaxia (Ming Tsuang and colleagues), prodromal symptoms (Barbara Cornblatt and colleagues), and issues related to genetic counseling (Debby Tsuang and colleagues).

Finally, the last section looks ahead to the near future of prevention research from two vantage points. One involves representative neurochemical areas that are relevant for schizotaxia research, but are in need of additional investigation

(William Stone and colleagues), and the other explores the prospects of molecular biology for advancing the goals of prevention and early intervention (Will Carpenter and James Koenig).

Early Clinical Intervention and Prevention of Schizophrenia explores the multidimensional nature of the liability to schizophrenia, often in the absence of psychosis or even a schizophrenia-related clinical diagnosis. Although prodromal or psychotic symptoms are already targets of active investigations, it is clear that pre-prodromal intervention based on clinical symptoms or cognitive deficits remains premature. Yet, as many of the authors in this volume demonstrate, the field is at the point of mapping strategies and validating intervention targets. Together with current efforts to attenuate prodromal and incipient psychotic symptoms, these developments bring us closer to the threshold of prevention studies. It is hoped that the multidimensional and interdisciplinary description of these efforts will benefit everyone interested in the prevention of schizophrenia, and more broadly, anyone interested in the prevention of major mental disorders.

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