

Introduction

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CONTROVERSIES AND NEW DIRECTIONS

Although the existence and diagnostic boundary of childhood bipolar disorder has been the focus of substantial controversy (see Chapter 2, this volume), there is evidence of a progressively growing consensus on both the existence of child mania and on the vicissitudes of age-specific research in this area (National Institute of Mental Health Research Roundtable on Prepubertal Bipolar Disorder, 2001; hereafter cited as NIMH Roundtable, 2001). The growing interest in this area has been demonstrated by the increasing number of federally funded projects on bipolar disorder in children and by the diverse areas these projects cover, including phenomenology, natural history, family studies, offspring, epidemiology, neuroimaging, treatment, and preclinical studies, as outlined in the NIMH Roundtable (2001). This book attempts to provide state-of-the-art understanding in the domains of epidemiology, diagnosis and natural history, neurobiology and genetics, and treatment.

WHY CONCEPTUALIZE CHILD AND EARLY ADOLESCENT BIPOLAR DISORDER?

As noted in the NIMH Roundtable (2001), regardless of the phenotype (conservative DSM-IV vs. broadly defined bipolar disorder not otherwise specified), there is agreement that prepubertal bipolar disorder is a chronic, mixed manic, continuously cycling disorder. Furthermore, the diagnostic and natural history similarity of prepubertal bipolar disorder to early adolescent bipolar disorder has been reported by Geller and colleagues (see

Chapter 2, this volume). In addition, many experts in the field view late-adolescent-onset bipolar disorder as phenomenologically similar to adult-onset bipolar disorder. In this regard, the NIMH-funded multisite study of the treatment of late-teenage-onset and adult-onset bipolar disorder, Systematic Treatment Enhancement of Bipolar Disorder (STEP-BP) includes subjects from age 15. Therefore, there is a growing consensus that prepubertal and early adolescent bipolar disorder share similar characteristics.

ORGANIZATION OF THIS BOOK

The chapters comprising this book can be divided into three sections. The first section focuses on the *diagnosis, natural history, and longitudinal course* of childhood and early adolescent bipolar disorder. In Chapter 1, Lewinsohn, Seeley, and Klein discuss their findings regarding the epidemiology, clinical characteristics, and outcome of syndromal and subsyndromal adolescent bipolar disorder. They also review their studies of the family history of psychopathology in probands with adolescent bipolar disorder. Their studies provide important insights into the risk of suicidality in early-onset bipolar disorder and the poor outcome associated with subsyndromal bipolar disorder in adolescents. Geller and colleagues, in Chapter 2, review their pioneering research examining the clinical characteristics and outcome of a prepubertal and early adolescent bipolar disorder (PEA-BP) cohort. One of the primary questions confronting the field in the early 1990s was whether children with mania were just children with “severe attention-deficit/hyperactivity disorder.” Geller and colleagues compared their well-characterized PEA-BP cohort with a group of children with attention-deficit/hyperactivity disorder. The results of this study, which enlightened the field as to the differences in clinical characteristics between these populations, are described in Chapter 2. Additionally, they review the development of their Washington University in St. Louis Kiddie Schedule for Affective Disorders and Schizophrenia (WASH-U-KSADS), a modified version of the K-SADS, designed to elicit age-specific diagnostic criteria for mania. The WASH-U-KSADS is now the most widely used diagnostic assessment instrument for pediatric bipolar research. Finally, Chapter 2 addresses the prognosis and outcome of these children and raises questions for future research.

In Chapter 3, DeJong and Frazier review the relationships among early-onset bipolar disorder and the pervasive developmental disorders. Specifically, they review the phenomenological characteristics, genetics, and pharmacological treatments for children and adolescents with co-occurring pervasive developmental disorders and early-onset bipolar disorder. Finally, DeJong and Frazier describe several illustrative cases that emphasize the importance of identifying the presence of a mood disorder in

a child with a pervasive developmental disorder. In Chapter 4, Papolos reviews the common comorbidities associated with early-onset bipolar disorder. Several possible explanations for the high co-occurrence between early-onset bipolar disorder and attention-deficit/hyperactivity disorder, disruptive behavior disorders, anxiety disorders, and substance use disorders are discussed. Additionally, Chapter 4 describes the methodological complications of studying comorbidities in pediatric bipolar disorder and Papolos suggests several ways in which this field can move forward. In the final chapter of this section, Chapter 5, Chang and Steiner review research involving children and adolescents of parents with bipolar disorder. This population provides an important opportunity for investigating the prodromal manifestations of early-onset bipolar disorder. Chang and Steiner provide an overview of the significance of bipolar offspring studies, discuss the methodological difficulties in studying bipolar offspring, summarize the results of bipolar offspring studies completed to date, and suggest future directions for this field of study. They also address the importance of identifying psychological and biological markers for illness development. Finally, the authors discuss preliminary results from two targeted early intervention studies.

The second section of this book focuses on the *neurobiology and genetics* of early-onset bipolar disorder. Although this field is in its infancy, this section provides important insights into innovative research that, in the near future, may clarify the biological basis of early-onset bipolar disorder. In Chapter 6, Farber and Newcomer examine the effects of *N*-methyl-D-Aspartate (NMDA) receptors and consider the possible role of NMDA receptor hypofunctioning in the pathophysiology of idiopathic psychotic disorders, paying particular attention to the relationship between brain maturation and development and NMDA receptor hypofunctioning. The authors propose that NMDA hypofunctioning may result in chronic severe symptoms complicated by ongoing structural brain changes and clinical deterioration. Finally, the authors discuss the implications of certain protective drugs that arrest the neurotoxicity associated with NMDA hypofunction, including olanzapine, clozapine, lamotrigine, α_2 -adrenergic agonists, and perhaps antimuscarinic agents. In Chapter 7, DelBello and Kowatch examine novel neuroimaging techniques and their potential utility for investigating the neurophysiological basis of early-onset bipolar disorder. The authors also review the literature of neurostructural and neurofunctional abnormalities in children, adolescents, and adults with bipolar disorder and suggest that frontal-subcortical abnormalities may be present in children and adolescents with bipolar disorder. In Chapter 8, Bhangoo, Deveney, and Leibenluft examine the neural components of emotional processes and discuss how relevant concepts of affective neuroscience can be applied to childhood bipolar disorder. The authors also discuss methods that can be used to study theories of emotion and mood, focusing

on the psychophysiological correlates of emotion that are particularly relevant to the study of early-onset bipolar disorder. In Chapter 9, Soto and Murphy use the example of PANDAS (pediatric autoimmune neuropsychiatric disorders associated with streptococcus) to describe a model for childhood neuropsychiatric illnesses with an immune system etiology. The authors also examine the role of novel therapeutic agents if the presence of an immune-mediate pathophysiology is determined for pediatric bipolar disorder and suggest directions for future research in this area. In Chapter 10, Rao discusses the relationship between circadian dysregulation and bipolar disorder and the hypothesized mechanisms that underlie these disturbances. Sleep studies provide one method for studying these disturbances. In this chapter, EEG sleep changes in unipolar and bipolar disorders are summarized, and hypothesized mechanisms for these EEG sleep changes are proposed. Finally, future areas of sleep research in pediatric bipolar disorder are suggested. In the final chapter of this section, Chapter 11, Badner reviews family, twin, and adoption studies involving bipolar probands and concludes that there is strong evidence for a genetic basis for bipolar disorder. Furthermore, the data reviewed suggest that childhood-onset affective disorders share familial factors in common with adult-onset affective disorder and do not represent an etiologically distinct group.

The third and final section of this book focuses on treatment and other aspects of support that may be provided to children and adolescents with bipolar disorder and their families. In the first chapter of this section, Chapter 12, Ryan summarizes pharmacological treatment options for this population and studies supporting their use. There is a paucity of controlled pharmacological data for children and adolescents with bipolar disorder. Future controlled trials are needed to investigate the efficacy of lithium, antiepileptic agents, and atypical antipsychotics in this population, as well as treatment options for children and adolescents with bipolar disorder and co-occurring disorders.

Chapter 13 emphasizes the importance of psychosocial treatments for children and adolescents with bipolar disorder. Specifically, in this chapter Goldberg-Arnold and Fristad describe the development of and preliminary results from a child group therapy program, developed as part of a multi-family psychoeducation program for families of preadolescent children with bipolar disorder. In Chapter 14, Fristad and Goldberg-Arnold raise the important issue of including the entire family in the treatment of patients with early-onset bipolar disorder. They outline several specific and practical family intervention strategies for helping families cope with a child with bipolar disorder. In the final chapter of this section and of the book, Hellander, Sisson, and Fristad review the literature on caregiver burden and how various forms of support can help families of children with bipolar disorder. They also provide a unique perspective on the development of a Internet-based support group for families of bipolar children, the

Child & Adolescent Bipolar Foundation, which was founded in 1999 by parents who met in early online support groups. The authors also focus on the Internet as an emerging medium for providing support services and describe the Internet's potential to create and sustain a supportive community for families raising children diagnosed with, or at risk for, bipolar disorder.

REFERENCE

National Institute of Mental Health Research Roundtable on Prepubertal Bipolar Disorder. (2001). *Journal of the American Academy of Child and Adolescent Psychiatry*, 40, 871–878.

