Bipolar Disorder: Clinical and Neurobiological Foundations

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## Contents

Preface vii  
List of Contributors ix  

1 From Mania to Bipolar Disorder  
David Healy  

2 Clinical Features and Subtypes of Bipolar Disorder  
Fred K. Goodwin and D.Z. Lieberman  

3 The Long-Term Course and Clinical Management of Bipolar I and Bipolar II Disorders  
Lewis L. Judd and Pamela J. Schettler  

4 Comorbidity in Bipolar Disorder: A Focus on Addiction and Anxiety Disorders  
Mark A. Frye and Giulio Perugi  

5 DSM-V Perspectives on Classification of Bipolar Disorder  
Jan Fawcett  

6 Update on the Epidemiology of Bipolar Disorder  
Kathleen R. Merikangas and Tracy L. Peters  

7 Suicide and Bipolar Disorder  
Zoltán Rihmer and Jan Fawcett  

8 Neurocognition in Bipolar Disorder  
Ivan J. Torres and Gin S. Malhi  

9 The Genius-Insanity Debate: Focus on Bipolarity, Temperament, Creativity and Leadership  
Hagop S. Akiskal and Karen K. Akiskal  

10 Economics of Bipolar Disorder  
R. Sabes-Figuera, D. Razzouk and Paul E. McCrone  

11 An Introduction to the Neurobiology of Bipolar Illness Onset, Recurrence and Progression  
Robert M. Post and Marcia Kauer-Sant’Anna  

12 Genetics of Bipolar Disorder  
Falk W. Lohoff and Wade H. Berrettini  

13 Structural Brain Imaging in Bipolar Disorder  
Paolo Brambilla and Jair C. Soares  

14 Functional Magnetic Resonance Imaging, Diffusion Tensor Imaging, and Magnetic Resonance Spectroscopy in Bipolar Disorder  
In Kyoon Lyoo and Perry F. Renshaw  

15 Functional Brain Imaging Studies in Bipolar Disorder: Focus on Cerebral Metabolism and Blood Flow  
John O. Brooks III, Po W. Wang and Terence A. Ketter  

16 Neurotransmitter Systems in Bipolar Disorder  
Marina Nakic, John H. Krystal and Zubin Bhagwagar  

17 Molecular Biology of Bipolar Disorder  
Ana Andreazza, Jun Feng Wang and Trevor Young  

18 Mitochondrial Dysfunction and Oxidative Stress  
Tadafumi Kato, Flavio Kapczinski and Michael Berk  

19 Neuroendocrinology of Bipolar Illness  
Timothy Dinan and Michael Bauer  

20 Circadian Rhythms and Sleep in Bipolar Disorder  
Greg Murray and Allison Harvey  

21 Treatment Adherence in Bipolar Disorder  
Jan Scott and Mary Jane Tacchi  

22 Acute Mania  
Paul E. Keck, Jr, Susan L. McElroy and John M. Hawkins
Preface

Bipolar disorder is a relatively recent concept, which emerged in the middle of the 20th century. However, bipolar disorder is not a new disease. Indeed, Aretaeus of Cappadocia, in his descriptions, captured the essence of the nature and course of mood changes of mania and depression almost 2000 years ago.

The objective of this book is to describe the clinical and neurobiological foundations of the modern concept of bipolar disorder as defined by the American Psychiatric Association’s Diagnostic Manual of Mental Disorders and the International Classification of Diseases. In order to capture both the American and the international perspectives, the editors deliberately chose authors from different continents for most chapters.

The book is divided into four sections. The first section covers the descriptive aspects of the disorder. This section begins with an historical overview of the evolution of the concept of bipolar disorder. While Dr. Healy admits that bipolar disorder is a distinct clinical entity, he argues that the boundaries of the modern concept of bipolar disorder have been shaped primarily by the interests of the industry over the past 15 years. The next two chapters review clinical features, course and outcome in the context of new data and suggest that depressive symptoms dominate the course of bipolar disorder and that the disorder is chronic for a significant proportion of patients. Comorbidity is the rule rather than an exception for bipolar patients and this chapter illustrates some of the common comorbidities patients with bipolar disorder experience. Dr. Fawcett then outlines the DSM-V process and some of the issues that the DSM-V will address with regard to classification of bipolar disorder in the next chapter. The remaining chapters in this section emphasize that bipolar disorder is common, associated with significant economic burden. This section also contains a fascinating review of the genius–insanity debate.

The biological aspects section begins with an overview of the neurobiology of bipolar disorder by Robert Post. Subsequent chapters address in greater detail some of the following questions: what is the current status with regard to the search for bipolar susceptibility genes? What brain regions and brain chemicals are altered in bipolar patients? Are changes in neurotransmitters and neurohormones still relevant or are changes in post-receptor signalling pathways more critical to the neurobiology of bipolar disorder? Is bipolar disorder associated with oxidative stress, mitochondrial dysfunction or alterations in biological rhythms?

Treatment adherence is a major challenge in the management of bipolar disorder. Thus, the section on management begins with an overview of reasons for non-adherence and strategies to improve adherence. This is followed by a series of chapters that describe the current status of the pharmacological management of various phases and subtypes of bipolar disorder. This section also contains chapters that review the role of novel treatments, somatic treatments, and safety monitoring, as well as the role of psychological treatments as adjuncts to pharmacotherapy.

The final section on special populations provides clinicians with the latest information and guidance on the management of bipolar disorders in women, children and the elderly.

We hope that this book will become a useful resource for psychiatrists and other health care professionals to improve their understanding and management of bipolar disorder.

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*Sadly, Elizabeth B. Weller died during preparation of the manuscript
From Pinel to Kraepelin

When the first asylums opened, around 1800, mania was a generic term for insanity. Philippe Pinel’s *Treatise on Insanity* that appeared in 1800 was accordingly named *Traité sur la Manie*.

For 2000 years before Pinel, the chief determinant of diagnosis in medicine lay in the visible presentation of the patient. These visible presentations could lead to reliable diagnoses of tumours, diabetes, catatonia, epilepsy and insanity. The visible presentations of insanity involved flushing, overactivity and maniacal behaviour. Mania was diagnosed in patients who were overactive and who might now be seen as having schizophrenia, depression, delirium, senility, imbecility and other conditions.

Pinel took a stand on the importance of science in medicine, and was the first to call for an Evidence Based Medicine. Faced with patients hospitalized for years, he was the first to incorporate the course of a patient’s disorders into his diagnostic considerations. He recorded outcomes where patients were treated or left untreated, and noting responses followed by relapses, argued that some disorders were periodic or recurrent and that the vast majority of available treatments made the underlying condition worse.

When a final and more complete version of his treatise was published in 1809, it distinguished in its title, *Traité Médico-Philosophique sur l’Aliénation Mentale ou la Manie*, between insanity in general and a new, more specific diagnosis of mania [1]. Once this distinction was made, and mania was separated out from idiocy dementia and melancholia, the rates of admission for mania settled at approximately 50% of all admissions in asylums in Europe and America until around 1900.

While asylum nomenclature remained relatively constant for a century, there was an evolution in the thinking about insanity. The idea that there might be a distinct mood faculty that could be disordered in its own right was put forward in the 1830s by one of Pinel’s pupils, Jean-Dominique Etienne Esquirol, who described profound sadness – lypemanie – as a distinct disorder.

The notion of a disease entity took shape in the 1850s when two of Esquirol’s pupils, Jean-Pierre Falret and Jules Baillarger, both described disorders that laid the basis for what became circular insanity. Falret outlined *folie circulaire*; Baillarger termed his disorder *folie à double forme* [2].

The idea that mania or insanity might give rise to protean manifestations had posed little difficulty, but as clinicians moved towards the concept of a disease entity, they had difficulties with the idea that two clinical states that looked so different might be presentations of the same underlying disease state. In their efforts to overcome these conceptual problems, both Falret and Baillarger posited a disorder with alternating cycles of mania and melancholia of fixed length and with fixed intervals between episodes. But crucially if neither the superficial features of mania nor the superficial features of melancholia accounted for the disorder, then some common ground between them must be responsible for the disorder. Some substrate must be diseased.

The new disorder was not one that commanded clinical attention. Both men conceded that what they were describing was a rare condition. The condition described was moreover at this point not clearly a mood disorder. Others described alternating or circular insanity. None of these states were bipolar affective disorder, as that term would be understood today.

The first to approach modern bipolar disorder was Karl Kahlbaum who in 1883 described cyclothymia. Where circular insanity was a psychotic disorder, with regular and stable features that led to degeneration, cyclothymia was for Kahlbaum a specific mood disorder from which patients could recover.

Kahlbaum also introduced disease course as a classificatory principle, but this was resisted. Most academics at the time expected a localization of clinical features in different brain areas to provide the key to unlocking the mysteries of mental illness rather than disease course. However disease course was used by Charcot to distinguish between hysteria and Tourette’s syndrome, and later to distinguish between Alzheimer’s and Creutfeld-Jacob disease.