Bipolar Disorders

Basic Mechanisms and Therapeutic Implications

Third Edition

Bipolar Disorders

Basic Mechanisms and Therapeutic Implications

Third Edition

Edited by

Jair C. Soares
The University of Texas Health Science Center in Houston, TX, USA

and

Allan H. Young
King's College London, London, UK

CAMBRIDGE
UNIVERSITY PRESS

CAMBRIDGE
UNIVERSITY PRESS

Contents

Contents

Contributors

Izabela Guimarães Barbosa

Neuroscience Branch, Interdisciplinary Laboratory of Medical Investigation, School of Medicine, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

Moisés Evandro Bauer

Laboratory of Immunosenescence, Institute of Biomedical Research, Pontifícia Universidade Católica do Rio Grande do Sul, Brazil

Carrie E. Bearden, PhD

Semel Institute for Neuroscience and Human Behaviour, Departments of Psychiatry and Biobehavioral Sciences and Psychology, University of California, Los Angeles, California, USA

Francesco Benedetti

Department of Clinical Neurosciences, Scientific Institute and University Vita-Salute San Raffaele, Milan, Italy

Francine M. Benes, MD PhD

Director of Laboratory for Structural and Molecular Neuroscience, Director of Harvard Brain Tissue Resource Center, McLean Hospital, William P. and Henry B. Test Professor of Psychiatric Neuroscience, Harvard Medical School, Boston, Massachusetts, USA

Charles L. Bowden, MD

Department of Psychiatry, University of Texas Health Science Center at San Antonio, San Antonio, Texas, USA

Melissa A. Brotman

Section on Bipolar Spectrum Disorders, Emotion and Development Branch, National Institute of Mental Health, Department of Health and Human Services, National Institutes of Health, Bethesda, Maryland, USA

Danielle S. Cha

Mood Disorders Psychopharmacology Unit, University Health Network, University of Toronto, Toronto, Canada

Alexander W. Charney

Icahn School of Medicine at Mount Sinai, New York, New York, USA

Dennis S. Charney

Icahn School of Medicine at Mount Sinai, New York, New York, USA

Alessandro Colasanti

Centre for Affective Disorders, Department of Psychological Medicine, the Institute of Psychiatry, King's College London, London, UK

Gabriela Delevati Colpo, PhD

Center for Molecular Psychiatry, Department of Psychiatry and Behavioral Sciences, The University of Texas Medical School at Houston, Houston, TX, USA

Sara Dallaspezia

Department of Clinical Neurosciences, Scientific Institute and University Vita-Salute San Raffaele, Milan, Italy

Daniel P. Dickstein

Pediatric Mood, Imaging and Neurodevelopment Program, Department of Psychiatry and Human Behavior, Brown University Alpert Medical School and Bradley Hospital, East Providence, Rhode Island, USA

Brent Forester

Department of Psychiatry, Harvard Medical School and MacLean Hospital, Belmont, Massachusetts, USA

Sophia Frangou, MD PhD

Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, New York, USA

Contributors

Gabriel Rodrigo Fries, PhD
Federal University of Rio Grande do Sul, UFRGS, Porto Alegre, Brazil

Mark A. Frye, MD
Department of Psychiatry and Psychology, Mayo Clinic Depression Center, Mayo Clinic, Rochester, Minnesota, USA

Ariel G. Gildengers
Department of Psychiatry, University of Pittsburgh School of Medicine and Western Psychiatric Institute and Clinic, Pittsburgh, Pennsylvania, USA

David C. Glahn, PhD
Department of Psychiatry, Yale University School of Medicine, Hartford, Connecticut, USA

Flávio Kapczinski, MD PhD
Center for Molecular Psychiatry, Department of Psychiatry and Behavioral Sciences, The University of Texas Medical School at Houston, Houston, TX, USA

Martin J. Lan, MD PhD
Department of Psychiatry, Columbia University College of Physicians and Surgeons, New York, New York, USA

Ellen Leibenluft
Section on Bipolar Spectrum Disorders, Emotion and Development Branch, National Institute of Mental Health, Department of Health and Human Services, National Institutes of Health, Bethesda, Maryland, USA

J. John Mann, MD
Department of Psychiatry, Columbia University College of Physicians and Surgeons, New York, New York, USA

Rodrigo B. Mansur
Mood Disorders Psychopharmacology Unit, University Health Network, University of Toronto, Toronto, Canada

R. Hamish McAllister-Williams
Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, UK

Roger S. McIntyre
Mood Disorders Psychopharmacology Unit, University Health Network, University of Toronto, Toronto, Canada

Thomas Daniel Meyer, PhD
Department of Psychiatry and Behavioral Sciences, University of Texas Health Science Center, Houston, Texas, USA

Seharish Moughal
Icahn School of Medicine at Mount Sinai, New York, New York, USA

Trevor R. Norman
Department of Psychiatry, Austin Hospital, University of Melbourne, Heidelberg, Victoria, Australia

Olaoluwa O. Okusaga, MD MScPHR
Harris County Psychiatric Center, University of Texas, Houston, Texas, USA

Michael J. Ostacher, MD MPH MMSc
Department of Psychiatry, Veterans Affairs, Palo Alto Health Care System, Palo Alto, California, USA

Robert M. Post, MD
Clinical Professor of Psychiatry, George Washington University, Washington, DC, USA

Joshua D. Rosenblat
Mood Disorders Psychopharmacology Unit, University Health Network, University of Toronto, Toronto, Canada

Marsal Sanches, MD PhD
Department of Psychiatry and Behavioral Sciences, University of Texas Houston Medical School, Houston, Texas, USA

Sehrish Sayed
Icahn School of Medicine at Mount Sinai, New York, New York, USA

Banafsheh Sharif-Askary
Section on Bipolar Spectrum Disorders, Emotion and Development Branch, National Institute of Mental Health, Department of Health and Human Services, National Institutes of Health, Bethesda, Maryland, USA

Jair C. Soares, MD PhD
Department of Psychiatry and Behavioral Sciences, University of Texas Health Science Center, Houston, Texas, USA

Laura Stertz, PhD
Center for Molecular Psychiatry, Department of Psychiatry and Behavioral Sciences, The University of Texas Medical School at Houston, Houston, TX, USA

Contributors

Paul Stokes, MB ChB BSc (Hons) MRCPsych DIC PhD
Centre for Affective Disorders, Department of Psychological Medicine, Institute of Psychiatry, King's College London, London, UK

James Stone
Centre for Affective Disorders, Department of Psychological Medicine, Institute of Psychiatry, King's College London, London, UK

Sivan Subburaju, PhD
Program in Structural and Molecular Neuroscience and Harvard Brain Tissue Resource Center, McLean Hospital, Department of Psychiatry (Neuroscience), Harvard Medical School, Boston, Massachusetts, USA

Trisha Suppes, MD PhD
Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, California, USA

Antonio Lucio Teixeira
Associate Professor of Internal Medicine, Neurology and Psychiatry, Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

Consuelo Walss-Bass, PhD
Associate Professor, University of Texas Health Science Center, Department of Psychiatry and Behavioral Sciences, Houston, Texas, USA

Allan H. Young
Department of Psychological Medicine, the Institute of Psychiatry, King's College London, London, UK

Robert C. Young, MD
Professor, Department of Psychiatry, Weill Cornell Medical College and New York Presbyterian Hospital, Westchester Division, White Plains, New York, USA

ix

Preface

Over the past two decades, fostered by developments in the clinical neurosciences, considerable progress has occurred in the understanding of brain function and abnormalities involved in neuropsychiatric disorders. Despite this growing area of research, available information on the basic brain mechanisms of bipolar and unipolar mood disorders is still limited. In recent years, this important gap has been increasingly addressed. The enormous public health importance of bipolar disorder has been recognized and research initiatives have begun to elucidate its pathophysiology. These research initiatives will likely lead to breakthroughs in the understanding of causation and foster the development of novel treatments.

Of particular relevance and interest are developments in molecular biology and neuropsychopharmacology which provide new ways to study neuronal function and cell signaling. A focus on mechanisms of neuronal resilience and death, as well as inflammatory mechanisms and oxidative stress, has contributed exciting new hypotheses in recent years that are now being tested. Developments in neuroimaging have made possible the *in vivo* study of brain systems and pathways, as well as both neurotransmission and metabolic processes. Important tools from the field of genetics have become available and are being applied to further the understanding of mechanisms involved in bipolar disorder and intermediate phenotypes that may be linked to it. These novel research avenues have provided new dimensions in exploring the biological mechanisms involved in causation. These advances are gradually being translated into new approaches for the treatment of these severe mental illnesses.

To fill the gap in information related to basic mechanisms possibly involved and to try to build the bridge from basic research developments to benefits to our patients at the bedside, we are happy to present the third edition of our textbook, *Bipolar Disorders – Basic Mechanisms and Therapeutic Implications.* There is considerable research that has accumulated since our second issue was published in 2007 and we felt that 2016 would be a very appropriate time for our third issue to come out. This volume presents important contributions by the leaders in the particular areas of research pertinent to bipolar disorder. We have included chapters on genetics, neuroimaging, neuropsychopharmacology, oxidative stress and neuronal resilience, inflammatory mechanisms, psychosocial factors, childhood onset and late-life bipolar disorder, and several other important topics. The potential therapeutic implications of new research are emphasized throughout the book.

We are honored to have had the collaboration of this outstanding group of leading researchers and believe this volume will be a valuable resource for academicians and practitioners in the field of Psychiatry. It is presented as a complete and accessible reference to the most updated information on the biological basis and emerging therapeutics of bipolar disorder. It should be useful as supplemental reading for graduate and postgraduate courses on the neurobiology of mental illness. Mental health practitioners will find it useful as an updated source with the most recent research progress in this field. We hope you will share our excitement with these new developments which bring continued hope for more effective treatments to best help our patients and their families.

Jair C. Soares, M.D. and Allan H. Young, M.D.