

# Contents

<b>Foreword: Exciting Times</b>	<b>xv</b>
Jack Ende	
<b>Preface: Management of Psychiatric Disorders and Suicidal Behavior in the Twenty-First Century</b>	<b>xvii</b>
Leo Sher	
<b>The Role of Inflammation in the Pathophysiology of Depression and Suicidal Behavior: Implications for Treatment</b>	<b>1</b>
Gianluca Serafini, Alessandra Costanza, Andrea Aguglia, Andrea Amerio, Alice Trabucco, Andrea Escelsior, Leo Sher, and Mario Amore	
<p>Depression and suicidal behavior are 2 complex psychiatric conditions of significant public health concerns due to their debilitating nature. The need to enhance contemporary treatments and preventative approaches for these illnesses not only calls for distillation of current views on their pathogenesis but also provides an impetus for further elucidation of their novel etiological determinants. In this regard, inflammation has recently been recognized as a potentially important contributor to the development of depression and suicidal behavior. This review highlights key evidence that supports the presence of dysregulated neurometabolic and immunologic signaling and abnormal interaction with microbial species as putative etiological hallmarks of inflammation in depression as well as their contribution to the development of suicidal behavior. Furthermore, therapeutic insights addressing candidate mechanisms of pathological inflammation in these disorders are proposed.</p>	
<b>Fire and Darkness: On the Assessment and Management of Bipolar Disorder</b>	<b>31</b>
Katerina Nikolitch, Gayatri Saraf, Marco Solmi, Kurt Kroenke, and Jess G. Fiedorowicz	
<p>Bipolar disorder is characterized by recurrent mood episodes, affecting 1% to 2% of the population. Although its defining features are manic and hypomanic episodes, its course is dominated by depressive syndromes. Diagnosis can be challenging owing to symptom overlap with other disorders. Management goals include early and complete remission of acute episodes and the prevention of relapse between episodes. We present an overview of bipolar disorder and its subtypes, including algorithms and suggestions for screening, assessment, and management.</p>	
<b>Schizophrenia: One Name, Many Different Manifestations</b>	<b>61</b>
Justin Faden and Leslie Citrome	
<p>Schizophrenia is a disabling condition impacting approximately 1% of the worldwide population. Symptoms include positive symptoms (eg, hallucinations, delusions), negative symptoms (eg, avolition, anhedonia), and cognitive impairment. There are likely many different environmental and pathophysiologic etiologies involving distinct neurotransmitters and neurocircuits. Pharmacologic treatment at present consists of dopamine</p>	

receptor antagonists, which are reasonably effective at treating positive symptoms, but less effective at treating cognitive and negative symptoms. Nondopaminergic medications targeting alternative receptors are under investigation. Supportive psychosocial treatments can work in tandem with antipsychotic medications and optimize patient care.

### **Microbiome in Anxiety and Other Psychiatric Disorders**

73

Norman M. Spivak, Jonathan Haroon, Andrew Swenson, Scott A. Turnbull, Nolan Dang, Matthew Ganeles, Collin Price, Margaret Distler, Erika Nurmi, Helen Lavretsky, and Alexander Bystritsky

Initial studies suggested that the fluctuations in the quantity, variety, and composition of the gut microbiota can significantly affect disease processes. This change in the gut microbiota causing negative health benefits was coined dysbiosis. Initial research focused on gastrointestinal illnesses. However, the gut microbiome was found to affect more than just gastrointestinal diseases. Numerous studies have proven that the gut microbiome can influence neuropsychiatric diseases such as Parkinson's disease, Alzheimer's disease, and multiple sclerosis.

### **Post-traumatic Stress Disorder**

85

Addie N. Merians, Tobias Spiller, Ilan Harpaz-Rotem, John H. Krystal, and Robert H. Pietrzak

Post-traumatic stress disorder (PTSD) is characterized by symptoms of re-experiencing, avoidance, negative alterations in cognition and mood, and marked alterations in arousal and reactivity following exposure to a traumatic event. PTSD can be assessed by structured interviews and screening measures in psychiatric and nonpsychiatric settings. Evidence-based psychotherapies are the first-line treatment of PTSD, with cognitive behavioral therapies, such as prolonged exposure, cognitive processing therapy, and eye movement desensitization and reprocessing having the largest body and highest quality of evidence. Serotonin reuptake inhibitors are the first-line pharmacologic treatments for PTSD and are often used in conjunction with other therapeutic interventions.

### **From Mouse to Man: N-Methyl-D-Aspartic Acid Receptor Activation as a Promising Pharmacotherapeutic Strategy for Autism Spectrum Disorders**

101

Stephen I. Deutsch and Jessica A. Burket

The BALB/c mouse displays hypersensitivity to behavioral effects of MK-801 (dizocilpine), a noncompetitive N-methyl-D-aspartic acid (NMDA) receptor "open-channel" blocker, and shows both no preference for an enclosed stimulus mouse over an inanimate object and reduced social interaction with a freely behaving stimulus mouse. NMDA receptor agonist interventions improved measures of social preference and social interaction of the BALB/c mouse model of autism spectrum disorder (ASD). A "proof of principle/proof of concept" translational 10-week clinical trial with 8-week of active medication administration was conducted comparing 20 DSM-IV-TR-diagnosed older adolescent/young adult patients with ASD randomized to once-weekly pulsed administration (50 mg/d) versus daily administration of D-cycloserine (50 mg/d). The results showed that D-cycloserine, a partial glycine agonist, was well tolerated, the 2 dosing strategies did not differ, and

improvement was noted on the “lethargy/social withdrawal” and “stereotypic behavior” subscales of the Aberrant Behavior Checklist. NMDA receptor activation contributes to the regulation of mTOR signaling, a pathologic point of convergence in several monogenic syndromic forms of ASD. Furthermore, both NMDA receptor hypofunction and imbalance between NMDA receptor activation mediated by GluN2B and GluN2A-containing NMDA receptors occur as “downstream” consequences of several genetically unrelated abnormalities associated with ASD. NMDA receptor-subtype selective “positive allosteric modulators (PAMs)” are particularly appealing medication candidates for future translational trials.

### **Suicide: An Overview for Clinicians**

119

Leo Sher and Maria A. Oquendo

Most suicides have a diagnosable psychiatric disorder, most frequently, a mood disorder. Psychosocial issues and neurobiological abnormalities such as dysregulation in stress response systems contribute to suicidal behavior. All psychiatric patients need to be screened for the presence of suicidal ideation. Clinicians are expected to gather information about patient’s clinical features and to formulate decisions about patient’s dangerousness to self and the treatment plan. As psychiatric disorders are a major risk factor for suicide their pharmacologic and psychological treatment is of utmost importance to prevent suicide. Restriction of access to lethal means is important for suicide prevention.

### **Psychiatric Issues Among Health Professionals**

131

María Dolores Braquehais and Sebastián Vargas-Cáceres

COVID-19 has increased the interest in the wellbeing of health professionals (HPs) as they have experienced stress, loss, and fatigue-related symptoms. Research evidence from previous epidemics points to an increase in the prevalence of affective, anxiety, and addictive disorders among them. HPs are trained to care for others and to recover from severe stressors. However, they tend to neglect self-care and have difficulties in seeking appropriate help when need it. This new scenario becomes an opportunity to promote a new culture of professionalism whereby caring for the caregivers becomes a priority both at a personal and institutional level.

### **Overall goal of Cognitive-Behavioral Therapy in Major Psychiatric Disorders and Suicidality: A Narrative Review**

143

Gianluca Serafini, Alessandra Costanza, Andrea Aguglia, Andrea Amerio, Valeria Placenti, Luca Magnani, Andrea Escelsior, Leo Sher, and Mario Amore

Cognitive-behavioral therapy (CBT) is a form of psychological treatment that is based on the underlying assumption that mental disorders and psychological distress are maintained by cognitive factors, that is, that general beliefs about the world, the self, and the future contribute to the maintenance of emotional distress and behavioral problems. The overall goal of CBT is to replace dysfunctional constructs with more flexible and adaptive cognitions. The most relevant cognitive-behavioral techniques in clinical practice are: i. Cognitive Restructuring (also known as the ABCDE method) is indicated to support patients dealing with negative beliefs or thoughts. The different steps in the cognitive restructuring process are summarized by the letters in the ABCDE acronym that describe the different stages of

this coaching model: Activating event or situation associated with the negative thoughts, Beliefs and belief structures held by the individual that explain how they perceive the world which can facilitate negative thoughts, Consequences or feelings related to the activating event, Disputation of beliefs to allow individuals to challenge their belief system, and Effective new approach or effort to deal with the problem by facilitating individuals to replace unhelpful beliefs with more helpful ones. ii. Problem-Solving (also known as SOLVE) to raise awareness for specific triggers, and evaluate and choose more effective options. Each letter of the SOLVE acronym identifies different steps of the problem-solving process: Select a problem, generate Options, rate the Likely outcome of each option, choose the Very best option, and Evaluate how well each option worked. For example, a suicide attempt is reconceptualized as a failure in problem-solving. This treatment approach attempts to provide patients with a better sense of control over future emerging problems. iii. Re-attribution is a technique that enables patients to replace negative self-statements (eg, “it is all my fault”) with different statements where responsibility is attributed more appropriately. Furthermore, decatastrophizing may help subjects, especially adolescents decide whether they may be overestimating the catastrophic nature of the precipitating event, and by allowing them to scale the event severity they learn to evaluate situations along a continuum rather than seeing them in black and white. iv. Affect Regulation techniques are often used with suicidal adolescents to teach them how to recognize stimuli that provoke negative emotions and how to mitigate the resulting emotional arousal through self-talk and relaxation.

### **Depression and Suicidal Behavior in Adolescents**

169

Aliza Grossberg and Timothy Rice

Depression commonly onsets in adolescence, affecting approximately 1 in 4 female adolescents and 1 in 10 males in the United States. Adolescent depression is a significant risk factor for suicide, the cause of over a third of all American adolescent deaths. Adolescent depression is introduced alongside its developmental and gendered considerations with a focus on important risk factors of adolescent depression, including nonsuicidal self-injury, adverse childhood experiences, and substance abuse. Protective factors and contemporary special topics of the COVID-19 pandemic and social media use are reviewed. Therapeutic options and clinical barriers are highlighted before a summary of findings and conclusion.

### **Frailty: A Multidimensional Biopsychosocial Syndrome**

183

Carl I. Cohen, Rivka Benyaminov, Manumar Rahman, Dilys Ngu, and Michael Reinhardt

The original conceptual landscape of frailty has evolved into a complex, multidimensional biopsychosocial syndrome. This has broadened the field to now include social and behavioral scientists and clinicians from a wide range of specialties. This article aims to provide an updated overview of this conceptual change by examining the emerging definitions of physical, cognitive, social, and psychological frailty; the tools used for diagnosis and assessment of these domains; the epidemiology of the domains; their pathogenesis, risk factors, and course; frameworks for prevention and treatment; and unresolved issues affecting the field.