Preface

The first edition of *Neuroscience for the Mental Health Clinician* was published in 2003, just after the close of the National Institute of Mental Health's "Decade of the Brain." The U.S. Congress declared that "to enhance public awareness of the benefits to be derived from brain research, the Congress, by House Joint Resolution 174, has designated the decade beginning January 1, 1990, as the *Decade of the Brain* and has authorized and requested the President to issue a proclamation in observance of this occasion." The 1990s saw the emergence of neuroimaging and genetics as tools for research into mental disorders, and the first edition hinted at what might be on the horizon. I discussed dopamine genes for attention-deficit/hyperactivity disorder (ADHD), which regions of the brain might be involved in ADHD or affective disorder, and how psychopharmacological agents might exert their therapeutic effects. I mapped out hypothetical pathways of disease which, I hoped, would prove to be representative of the major mental disorders studied.

With the second edition, it is astonishing to see how much has changed in a little over a decade. Indeed, one only has to look at the 1990s-style webpage of the Decade of the Brain (*www.loc.gov/loc/brain*) and compare it to the webpage of the Human Connectome Project (*www.humanconnectomeproject.org*) to see the new, incredible breadth of contemporary brain research. If you have not heard of the Human Connectome Project, then you should wonder whether you might be as outdated as an old Compaq PC. Of course, you might fairly retort, "What does it matter?" After all, did the Decade of the Brain really produce any clinically relevant information? Are we now just looking at fancier websites? Perhaps, in 10 years we will be saying that the Connectome Project has been a big

disappointment. Why not just wait to learn about these things until someone discovers their true clinical relevance?

Before answering this question, I would like to give my personal perspective. My career has been unusual in that I have always been a practicing psychiatrist in addition to my research activities. When I began my academic career in the mid-1980s, I was primarily interested in ADHD itself. I joined other researchers who focused on finding "deficits" in norepinephrine or dopamine brain systems. Why the focus on these two chemicals? Because stimulant medications, the principal treatment for ADHD, blocked their uptake into neurons. We sought the answer by measuring the metabolites of norepinephrine and dopamine in urine (a technique that seems quaint in retrospect), but no clear result emerged. As I entered the field, I was responsible for developing the clinical ADHD program in our Division of Child and Adolescent Psychiatry. I saw 10–15 children with ADHD a week, either on my own or as a supervisor for our psychiatry residents. Many of these children and their families would go on to participate in my first research studies. I began to notice that many of these children with ADHD had anxiety disorders as well. This presented a problem: It was believed by clinicians at the time that these disorders were opposites of one another and that stimulant treatment made anxiety worse. Moreover, norepinephrine was believed to be elevated in anxiety. So how could ADHD and anxiety coexist if ADHD was caused by norepinephrine being too low and anxiety was caused by increased norepinephrine? Trying to answer this question set me on the study of comorbidity of other disorders with ADHD. Today, it is well accepted that ADHD is frequently comorbid with a wide range of psychiatric conditions (Biederman, Newcorn, & Sprich, 1991; Pliszka, 2009). It was my inquiry into the role of norepinephrine in behavior that led me to appreciate that each diagnosis in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) was not a stand-alone entity. Thus, I was able to expand my view of the disorder and the reach of treatment. By becoming more up to date in one's understanding of where neurobiology currently stands, it is possible to gain greater insight into the needs of one's patients.

I do not shy away from the fact that two decades of neurobiology research have not yielded a biological test for psychiatric disorder or produced a revolutionary treatment. "It's coming; this time we really mean it," is hardly a clarion call. When I entered psychiatry residency in 1981, we treated ADHD with short-acting stimulants, depression with tricyclic antidepressants, mania with lithium, and psychosis or aggression with "first-generation" antipsychotics such as haloperidol. Today, we treat ADHD with long-acting stimulants and depression with selective serotonin reuptake inhibitors (SSRIs). We have added anticonvulsant medications to the regimen for mood stabilization while using newer "second-generation" antipsychotics for psychosis, mood stabilization, and aggression. Patient

outcomes (except for a possibly reduced side-effect burden) are unchanged. This state of affairs should not make us cynical about brain research; it should make us redouble our efforts. Cancer research took 60 years of both trial and error and focused effort to reach the cure rates we have today (Zeng et al., 2015). I put this question to all my clinical audiences: Would you go to an oncologist who said, "I don't keep up with the basic science of cancer; I just wait till someone tells me what is clinically relevant"? Obviously, you would not. No mental health professional should adopt the cavalier position that "brain function isn't 'clinically relevant'; therefore, I really don't need to know about it." All clinicians, at the very least, need to be able to explain to their patients what the current hypotheses are about the biological aspects of mental illness. We should no more call them "chemical imbalances" than we would cite the medieval theory of humors, which laid the basis for the use of leeches and bleeding treatments well into the 18th century.

A glance at the table of contents shows that this edition has retained the structure of the first edition, but there has been a significant change in the theme and depth of each chapter. In the 20th century, the study of mental illness was still very much influenced by the "lesion" model of neurology. We thought in terms of which "gene" or which "brain region" was defective in a given disorder; furthermore, there was an implicit idea that each disorder defined by the DSM would have a unique pattern of brain dysfunction. While chapters are still organized by disorder, the new edition focuses on the key idea that psychiatric disorders are not neatly cleaved off from one another but share etiological factors and certain types of brain differences. I speak less of deficits in a given brain region and more about brain *networks*; that is, how do different brain regions interact with each other to produce cognition, emotions, and behavior? How can disturbances in these regions lead to psychopathology? A quick comparison of the figures from the first edition to this one clearly illustrates this: I moved away from the "circuit board" or A-to-B-to-C pathway illustration to show multiple, interacting regions.

A new emphasis in this edition is the growing awareness of how environment shapes both the structure and function of the brain. We have known for decades that gene and environment interact; what is new is the science of *epigenetics*. Environment can shape gene expression, such that the gene activity of even identical twins differs sharply after many years. This in turn has important effects on brain anatomy and function. A recent study shows that children's brain growth is correlated with years of parental education and family income (Noble et al., 2015). This does not mean that poor people are born with small brains; rather, the limited environment of a child born into poverty may stunt the epigenetic mechanisms that lead to optimal brain development. This is particularly relevant to the

study of the effects of child abuse and neglect. Our genes are the hardware; epigenetics is the software that runs the brain development process. How we raise our children affects them in a more profound way than we could ever imagine. It implies that the responsibility of society for mental illness is also far greater. As Charles Darwin himself observed, "If the misery of our poor be not caused by nature, but by our social institutions . . . then great is our sin."

In addition to epigenetics and a brain network approach, this edition includes more detailed discussions of attention, memory, and higher cognitive function. It describes the deeper understanding of the role of neurotransmitters in behavior and emotion that has emerged in the last decade. The biological role of stress in affective and anxiety disorders is elucidated. A separate, more detailed chapter on autism spectrum disorders is included.

I would like to acknowledge many people who have assisted me with this edition. First and foremost, I would like to thank my wife, Alice Narvaez, PhD, for her enormous emotional support throughout this process and her invaluable editing and proofreading of each chapter. At each step of the process, she has provided critical feedback and has helped me to be clearer in what I have sought to convey to the reader. My son, Andrew, was taking his introductory chemistry and biology courses as a freshman in college as I wrote this book. His hard work mastering his own coursework filled me with pride and made me optimistic about how his generation will use the advances discussed here.

Many of my colleagues and friends have supported and encouraged me over the years. I would like to thank my fellow faculty members in the Division of Child and Adolescent Psychiatry for their hard work and support during my 20 years as Division Chief: Brigitte Bailey, MD, Joseph Blader, PhD, Margaret Farrell, MD, Louise O'Donnell, PhD, Rene Olvera, MD, Thomas Matthews, MD, Kenneth Matthews, MD, Donna Roybal, MD, Jessica Sandoval, MD, Tracy Schillerstrom, MD, and James Stedman, PhD. The psychiatry residents and medical students of the University of Texas Health Science Center at San Antonio (UTHSCSA) have been an inspiration to me; a neurobiology seminar for them became the seeds from which this book grew.

As the writing of this book came to a close, I was appointed Chair of the Department of Psychiatry at the UTHSCSA. The mental health field faces many challenges; I have become more aware of this now that I have responsibility for many Department entities that treat people with severe and persistent mental illnesses. It is my hope that greater understanding of the neurobiology of mental illness will lead not only to advances in biological treatments but also to a more humane perspective on how mentally ill people should be treated in society.