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# TEXTBOOK OF BIOLOGICAL PSYCHIATRY

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**Edited By**

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Falk Center for Molecular Therapeutics, Department of Biomedical Engineering,  
Northwestern University, Evanston, Illinois

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Adjunct Professor of Psychiatry, Medical College of Ohio, Toledo


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# CONTENTS

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Foreword . . . . .	xv
Preface . . . . .	xix
Contributors . . . . .	xxi

## Part I FOUNDATIONAL CONCEPTS 1

### 1 BIOLOGICAL PSYCHIATRY SKETCHED—PAST, PRESENT, AND FUTURE 3

*Jaak Panksepp*

Overture	3
Historical Overview	5
Three Giants of the First Half of the 20th Century	7
Three Great Phases of 20th-Century American Psychiatry	9
About 1910–1940: The Meyerian Synthesis of a Holistic Psychobiology	9
World War II through the 1970s: The Psychoanalytic Era	10
Ultrapositivistic Psychopharmacology Era (1970–Present)	12
Dilemma of Psychiatric Diagnostics: DSMs and Beyond	17
Functions of Diagnostics	19
From Pathophysiology to Pathogenesis	20
Perennial Problem: Distinguishing Affective and Cognitive Processes	24
Coda: Intersection of 20th-Century Forces Leading to a 21st-Century Synthesis	28
References	29

### 2 IMAGING HUMAN EMOTIONS AND AFFECTIVE FEELINGS: IMPLICATIONS FOR BIOLOGICAL PSYCHIATRY 33

*Mario Liotti and Jaak Panksepp*

On the Nature of Emotions	33
Emotional Changes Following Brain Damage	36
Neuroimaging Studies of Emotion	39
Brain Changes as a Function of Emotional States	44
Reciprocity of Human Cortico-Limbic Activity	50
Basic Emotional Operating Systems of the Brain: Animal Studies	51
Generating Emotional Feelings through Upper Brainstem–Limbic and Cortical Interactions	59
Conclusions and Some Psychiatric Implications	65
References	66
<b>3 NEURAL SUBSTRATES OF CONSCIOUSNESS: IMPLICATIONS FOR CLINICAL PSYCHIATRY</b>	<b>75</b>
<i>Douglas F. Watt and David I. Pincus</i>	
Introduction	75
Dualism versus Emergent Properties	77
Nosology: Core versus Extended Consciousness	78
Classical Work on the Neural Substrates of Consciousness	79
Recent Work on the Neural Substrates of Consciousness: Brief Overview of Anatomical, Connectivity, Neuromodulatory, and Neurodynamic Aspects	80
Case Study 1: Delirium—A Common Disorder of Attentional Function and Working Memory	84
Neuroanatomical Systems and Consciousness—Basic Lesion/Functional Correlates	88
Thalamic Systems	92
Cortical Systems	94
Two Case Studies of Mesodiencephalic Lesions	98
Neurodynamic Aspects of Consciousness	102
Summary Heuristics/Questions for Future Research	105
References	107
<b>4 STRESS, SLEEP, AND SEXUALITY IN PSYCHIATRIC DISORDERS</b>	<b>111</b>
<i>Terrence Deak and Jaak Panksepp</i>	
Introduction	111
Theoretical Framework for Understanding Stress Responsive Systems	112
Diathesis-Stress Models	114
Stress Responsive Systems	115



Integrative Role for Brain Cytokines	122
Sexuality and the Passions of the Brain	124
Sleep, Stress and the Restoration of Brain and Mind	130
References	136
<b>5 PSYCHOBIOLOGY OF PERSONALITY DISORDERS</b>	<b>145</b>
<i>Brian Knutson and Andreas Heinz</i>	
Overview	145
What Are Personality Disorders?	146
What Is Personality?	150
How Are Personality Disorders And Personality Related?	152
What Leads to “Disordered Personality”?	153
How Can “Disordered Personality” Be Treated?	157
Summary	159
Postscript: A View to the Future	159
References	160
<b>6 FUNCTIONAL NEUROIMAGING IN PSYCHIATRY</b>	<b>167</b>
<i>Johannes Tauscher, Nikolas Klein, and Shitij Kapur</i>	
Introduction	167
Magnetic Resonance Imaging	168
PET and SPECT	169
Studies of Cerebral Metabolism and Blood Flow	171
Neurotransmitter Imaging Studies	177
Future Directions and Challenges	186
References	187
<b>Part II CORE PSYCHIATRIC CHALLENGES</b>	<b>195</b>
<b>7 DEPRESSION: A NEUROPSYCHIATRIC PERSPECTIVE</b>	<b>197</b>
<i>Helen S. Mayberg</i>	
Diagnostic and Clinical Features	197
Treatment Options	201
Syndromal Markers	203
Biochemical Markers	206
Animal Models	208

Regional Brain Markers	208
References	221
<b>8 TREATMENT OF MOOD DISORDERS</b>	<b>231</b>
<i>Pedro L. Delgado and Paul Zarkowski</i>	
Overview	231
Classification	232
General Treatment Principles	235
Antidepressants	239
Somatic Treatments for Major Depression	250
Antimanic and Mood Stabilizers	252
Summary and Conclusions	259
References	259
<b>9 NEUROSCIENCE OF SCHIZOPHRENIA</b>	<b>267</b>
<i>Christine Pesold, Rosalinda C. Roberts, and Brian Kirkpatrick</i>	
Introduction	267
Diagnosis and Classification of Schizophrenia	268
Etiology	270
Environmental Risks	274
Course of Illness	276
Neuropathological Abnormalities	277
Neurocognitive Problems	285
Neuropsychiatric Syndromes	287
Neurochemical Abnormalities	287
Animal Models	289
Conclusion	292
References	293
<b>10 PHARMACOLOGICAL TREATMENT OF SCHIZOPHRENIA</b>	<b>299</b>
<i>Rajiv Tandon and Michael D. Jibson</i>	
Introduction	299
Targets of Pharmacological Treatment	300
Pharmacological Treatment	302
Course of Treatment	306

Combining Several Medications	309
Future Trends	311
Conclusion	315
References	315
<b>11 PSYCHOBIOLOGY OF POSTTRAUMATIC STRESS DISORDER</b>	<b>319</b>
<i>Bessel A. van der Kolk</i>	
Introduction	319
Psychobiology	324
Psychophysiological Effects of Trauma	325
Lessons from Neuroimaging	330
Implications for Treatment	335
Conclusions	338
References	338
<b>12 NATURE AND TREATMENT OF PANIC DISORDER</b>	<b>345</b>
<i>Fredric N. Busch and Barbara L. Milrod</i>	
Defining the Syndrome of Panic Disorder	345
Course of Panic Disorder	347
Basic Models of the Etiology of Panic Disorder	348
Treatment of Panic Disorder	354
Long-Term Outcome of Treatment Trials for Panic Disorder	359
References	361
<b>13 NATURE AND TREATMENT OF OBSESSIVE-COMPULSIVE DISORDER</b>	<b>367</b>
<i>Lisa A. Snider and Susan E. Swedo</i>	
Introduction	367
Epidemiology	368
Clinical Presentation	370
Comorbidity	372
The OCD Spectrum	373
Neurobiology	375
Treatment	382
Summary	385
References	385

<b>14</b>	<b>BIOLOGICAL BASIS OF CHILDHOOD NEUROPSYCHIATRIC DISORDERS</b>	<b>393</b>
	<i>Bradley S. Peterson and Jaak Panksepp</i>	
	Introduction	393
	Pervasive Developmental Disorders and Specific Genetic Syndromes	394
	Childhood-Onset Schizophrenia	408
	Disorders of Impulse Control	409
	Conclusions	419
	References	420
	Further Readings	435
 <b>15</b>	 <b>AGING AND DEMENTIA</b>	 <b>437</b>
	<i>Mark T. Wright, A. John McSweeney, and Amy Kieswetter</i>	
	History	437
	Cognition and Memory in Normal Aging	439
	Mild Cognitive Impairment	443
	Definition of Dementia	448
	Diagnosis of Dementia	450
	Some Major Causes of the Syndrome of Dementia	451
	Alzheimer's Disease	452
	Frontotemporal Dementia	461
	Vascular Dementia	467
	Dementia with Lewy Bodies	471
	Conclusions	475
	References	476
 <b>Part III</b>	 <b>FUTURE PROSPECTS</b>	 <b>487</b>
 <b>16</b>	 <b>EMERGING NEUROSCIENCE OF FEAR AND ANXIETY: THERAPEUTIC PRACTICE AND CLINICAL IMPLICATIONS</b>	 <b>489</b>
	<i>Jaak Panksepp</i>	
	Introduction	489
	Subcortical FEAR System of the Mammalian Brain: The "Royal Road" to Understanding the Nature of Angst	492
	Treatment of Anxiety in Clinical Practice	499
	Dispersion and Functions of Fear Systems in the Brain: Continuing Studies of the Neuroanatomy of FEAR	505

Experiential-Affective Attributes of Fear and Anxiety	506
Concluding Remarks	511
References	512
<b>17 SOMATIC TREATMENTS IN PSYCHIATRY</b>	<b>521</b>
<i>Ziad Nahas, Jeffrey P. Lorberbaum, Frank A. Kozel, and Mark S. George</i>	
Introduction	521
Electroconvulsive Therapy	522
Magnetic Seizure Therapy	525
Transcranial Magnetic Stimulation	526
Vagus Nerve Stimulation	532
Deep Brain Stimulation	536
Psychiatric Neurosurgery	537
Future Directions	539
References	540
<b>18 PSYCHOANALYSIS AND PSYCHOPHARMACOLOGY: ART AND SCIENCE OF COMBINING PARADIGMS</b>	<b>549</b>
<i>Marcia Kaplan</i>	
Introduction	549
Definition of Psychoanalytic Concepts	550
Challenge of Combining Paradigms	552
Future Prospects	566
Conclusions	567
References	568
<b>19 DEPTH PSYCHOLOGICAL CONSEQUENCES OF BRAIN DAMAGE</b>	<b>571</b>
<i>Oliver H. Turnbull and Mark Solms</i>	
Introduction	571
Depth Neuropsychology and Issues of Methodology	573
Prevalence of Psychological Changes in Neurological Patients	575
Lesions to the Left Convexity	576
Ventromesial Frontal Lobes	579
Confabulation and the Neurobiology of Emotion Systems	582
Lesions to the Right Convexity	585

Conclusion	590
References	591
<b>20 SOCIOPHYSIOLOGY AND EVOLUTIONARY ASPECTS OF PSYCHIATRY</b>	<b>597</b>
<i>Russell Gardner, Jr. and Daniel R. Wilson</i>	
Introduction	597
Relevant Evolutionary Concepts	598
Sociobiological Factors of Ultimate Causation	604
Psychiatric Pathogenesis as Communicational Disorder	607
Research on Substance Abuse and Social Rank Hierarchy	613
Preliminary Treatment Implications	618
Conclusions	620
References	620
<b>21 FUTURE OF NEUROPEPTIDES IN BIOLOGICAL PSYCHIATRY AND EMOTIONAL PSYCHOPHARMACOLOGY: GOALS AND STRATEGIES</b>	<b>627</b>
<i>Jaak Panksepp and Jaanus Harro</i>	
Introduction	627
Neuropeptide Medicines: Still Waiting in the Wings	630
Emotional Foundations of Psychiatric Disorders	632
Neuropeptides in Psychiatric Disorders	634
Affective Foundations of Psychiatric Disorders and the Neurochemical Coding of Emotions	636
Two Childhood Disorders: Debatable Examples of Neuropeptide and Neurobehavioral Approaches	645
Neurotrophins and Psychiatric Disorders	647
Conclusions	649
References	651
<b>Appendix A PHARMACODYNAMICS AND PHARMACOKINETICS</b>	<b>661</b>
<i>Jaanus Harro</i>	
Introduction	661
Pharmacodynamics: What Can the Drug Do to the Body?	662

Pharmacokinetics: What Can Happen to a Drug in the Body?	670
Drug interactions, Tolerance, and Dependence	678
For Further Reading	680

Index	683
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# FOREWORD

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This is not the first attempt to integrate biology with human behavior and mental illness. The Bible attributes emotional and cognitive functions to heart, bowels, and kidneys. The ancients favored a humoral view of temperament (sanguine, phlegmatic, choleric, and melancholic). Over the ages the many attempts to treat mental illness have included physical and medicinal measures: purging, hydrotherapy, galvanic stimulation, and many other strange interventions, in the belief that doing something to the body would exorcise mental illness.

With the discovery of hormones, their effects on body, mind, and behavior—both normal and abnormal—were studied in the hope that they would be therapeutically useful. Early electroencephalographic investigation was expected to give us easy access to the functions of the brain and mind, but instead revealed disappointingly little information about mental illness and, in fact, about mental function in general. Only in the mid-20th century did Adolf Meyer promote a biological psychiatry that brought everything that was known to be relevant to mental health and illness to bear upon psychiatric diagnosis and treatment.

Sigmund Freud, who was best known for his original and perceptive insights into the psychology of mental illness, in fact maintained a consistent interest in biology. From the outset he argued that the same neural systems and functions that, in illness, give rise to the signs and symptoms of neurological disease, also bring about the signs and symptoms of mental illness. In 1891, Waldeyer gave final form to the neuron theory. Freud enthusiastically embraced it as a possible basis for what he called a “scientific psychology,” resulting in an uncompleted work, later known as the Project for a Scientific Psychology. He abandoned that effort when he realized that it was a will o’ the wisp, an illusory scheme, based on verbal constructs rather than neural mechanisms. Biological psychiatry, as it became fully biologized, has also abandoned many ambiguous mental constructs. Now a key challenge is how to bring those subtle attributes of the brain-mind, such as affects, into the neurobiological arena. One credible way is to try to link the visually observable instinctual apparatus of animals to affective processes.

Freud’s concept of drive was closely aligned with the ethologic concept of instinct; he attributed qualities to the drive that resemble closely those commonly associated with instinct. He saw instinct as “a concept on the frontier between the mental and

the somatic, . . . the psychical representative of the stimuli originating from within the organism and reaching the mind.” (*Instinct and Their Vicissitudes*, 1915, p. 121–122, *Standard Edition*) Running like a red thread throughout his work was the concept of *energy*, which always remained poorly defined. That too was a border concept: On the one hand, it was psychic energy; on the other hand it anticipated that medications still to be discovered in 1939, the year of his final statement, would exert their therapeutic effect by influencing this psychic energy.

Early intimations of a direct relation between the brain and hallucinated images and emotions were disclosed by the studies of the effects of direct stimulation of the exposed human brain by Wilder Penfield and his disciples in the middle of the 20th century. Soon thereafter, psychedelic and other psychoactive drugs revealed a chemically based mental apparatus with which neither scientific psychiatry nor psychology has come to terms.

It was soon after World War II that modern neuroscientific studies were initiated and rapidly developed momentum. Applied neuroscience (i.e., psychopharmacology) exerted its initial impact on a clinical psychiatry that had yet to become fully biologized. Though they had been preceded by the barbiturates that, in their day, had proved very useful, the newer agents now exhibited antipsychotic and mood-correcting powers. When the possibility of affecting mental illness chemically became clear, the drug companies addressed the problem with their formidable resources and in rapid succession introduced new variants of the basic therapeutic agents. Although the psychiatric profession accepted and employed these medications enthusiastically, the early literature exhibited little interest in using psychopharmacologic experience as a point of entry for a neuroscience of mental illness. The amazing development of molecular neuropharmacology recently has catalyzed that coordination.

The present volume represents a landmark in this developing trend. Trained as a behavioral neuroscientist and psychologist, editor Jaak Panksepp is knowledgeable in the field of psychoanalysis and experienced in practical psychotherapy. He has actively pursued reliable knowledge about brain function in its relation to behavior through careful animal experiments. He proceeds from the assumption that affect is the central variable in human behavior, to which other features are secondary. His 1998 work, *Affective Neuroscience*, is becoming one of the scriptures of the third revolution in 21st-century psychiatry. I consider psychoanalytic psychiatry the first, psychopharmacologic psychiatry the second, and a functional neuroscientific psychiatry the third.

In *Affective Neuroscience*, Panksepp examined the several instinctual systems, their affective correlates, and the autonomic and physiologic systems that subserve them. The neurochemistries involved also provided points of correlation with established and potentially new pharmacologic strategies. His was a novel and original approach to human behavior that permitted clinicians like myself a view of the opportunities and the promise of the neuroscientific approach to psychiatry.

In this *Textbook of Biological Psychiatry*, Panksepp fulfills this promise. I draw the reader’s attention especially to his introductory chapter in which he points the way to the elusive synthesis of studies of mind and brain, focusing on affect as the essential

and functional link. This emphasis is both timely and ironic since affect had been remote from the central interest of both psychoanalysts and neuroscientists.

For this endeavor, he has assembled a group of scientists and clinicians and invited them to apply contemporary neuroscience to psychiatric issues. This coordination of Panksepp's persistence and brilliance along with the insights of his carefully selected collaborators will afford a new, practical understanding of biological psychiatry, at once imaginative and realistic.

Mortimer Ostow, M.D., Med. Sc. D.  
President, Psychoanalytic Research and Development Fund



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# PREFACE

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This work was initiated with the aim of bringing together the traditions that have helped create modern biological psychiatry. The hope was to craft a perspective that could help project our thinking fruitfully into the future. During the past few decades, we have learned to quantify normal and abnormal brain functions at a level of precision unimaginable just a generation ago. However, progress in biological psychiatry is also based on new theoretical perspectives, for it is only through theory that we can envision what may emerge on the horizon of knowledge. Of course, theory can also be a lens that distorts reality.

Our aim was to seek the middle ground—a balance of facts and theories, as well as consideration of both clinical and preclinical perspectives. My hope is that this text will be useful for students, teachers, and practitioners, as well as the scientists who harvest the basic knowledge from which future understanding must emerge. I owe a debt of gratitude to the many contributors who took precious time from their busy schedules to summarize the important themes covered in this book. The only regret I have is that space constraints made it impossible to treat all topics as fully as they deserve. Luna Han, the acquisition editor for this contribution, exhibited remarkable forbearance and did not outwardly waver in her faith that the project would reach completion in a reasonably timely manner. That proved to be a challenge for many.

A special word of gratitude goes to my wife Anesa who read and commented extensively on the entire text. Each of the chapters underwent at least one major revision to optimize style and coverage, and several underwent cycles of intellectual adventure for both the contributors and editors. But even where the needs of the book and the desires of authors briefly clashed, the middle road was eventually found. Jeff Burgdorf, Casey Cromwell, and Nikki Gordon also provided assistance at several critical phases of the project. I thank all for their contributions.

We wish to dedicate this text to the many pioneers, past and present, who have devoted their lives to understanding the normal and abnormal functions of the human mind. Many now appreciate that such a quest cannot be completed unless we also try to understand the brains and minds of other creatures. Indeed, some of the most interesting research on mind, brain, and behavioral relations has been emerging from animal research conducted in departments of psychiatry and neurology. This is a tradition in which all of the three giants—Emil Kraepelin, Adolf Meyer, and Sigmund Freud—to

whom we dedicate this volume were immersed at some point in their illustrious careers. Their portraits are used with the permissions, respectively, of The University of Tartu Library, The Adolf Meyer Library of Medicine at Johns Hopkins University, and the Freud Archive, London.

Although each of these pioneers started with physiological and neurological interest, their intellectual paths eventually diverged. However, because of historical and intellectual circumstances that emerged during the 20th century (as summarized in Chapter 1), all hewed paths that made contributions to future efforts to blend mind, brain, and body perspectives to understanding mental disorders. The whole person is no less important than the dizzying arrays of parts of which he or she is composed. Below the surface features of mental phenomena are mechanisms with which we must become conversant in order to make progress, never forgetting that the emergent whole is greater than the parts. This book was constructed with such perspectives in mind, and thank everyone that contributed to this effort.

*Jaak Panksepp*  
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*J.P. Scott Center for Neuroscience, Mind and Behavior*



Emil Kraepelin  
(1856–1926)



Adolf Meyer  
(1866–1950)



Sigmund Freud  
(1856–1939)

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# Part I

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## FOUNDATIONAL CONCEPTS

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The background topics relevant to psychiatric disorders in biological terms is vast and typically includes neuroanatomy, neurophysiology, and neurochemistry. Since such approaches are remarkably well represented in various recent handbooks, and typically all substantive neuroscience courses, one more redundant effort in that direction would not be all that useful. Accordingly, we have used the limited space available to focus on topics that are more intimately related to psychological issues—the nature of emotionality, consciousness, stress, personality, and the brain imaging technologies that have changed the face of psychiatry in the past decade.

This decision was also fostered by the recognition that we have finally reached an era where the mind-brain barrier is beginning to dissolve. Although there are many ambiguities about what we may mean when we talk about “the mind,” most generous scholars accept that the dynamics of mind ride upon the dynamics of the brain, and we now know that for any psychotherapy to work, it must influence brain functions (Cozolino, 2002). Empirical demonstrations of this concept are growing rapidly, ever since Baxter and colleagues (1989) demonstrated that cognitive behavioral therapy could reduce the frontal cortical overactivity in obsessive-compulsive disorders. A few years ago the *Archives of General Psychiatry* published two back-to-back lead articles on how interpersonal therapy modified brain activities of depressed individuals in ways resembling those of modern serotonin-specific antidepressants (Brody et al., 2001; Martin, 2001).

Daniel J. Stern said it well in the foreword to Cozolino's (2002) treatise on the *Neuroscience of Psychotherapy*, as he indicated that clinicians immerse themselves "in the stories of individuals who come for help in feeling better. . . . Whatever the approach, lasting change in therapy occurs as a result of changes in the human mind. . . which involve changes in the functions of the brain. Exactly how the mind changes during the therapeutic process is the fundamental puzzle that the synthesis of neuroscience and psychotherapy seeks to solve" (p. ix). Stern emphasized the difficult but productive marriage between clinical and neuroscientific disciplines, highlighting how "psychotherapy emphasizes the importance of *subjective* experience and the power of relationships to transform the growing mind" while "neuroscience focuses on quantifiable, *objective* data and the scientific method to create models of mind and brain" (p. x). The interpenetration of neuroscientific knowledge and psychiatric practice is becoming much more than the impressive recitation of the great victories of the neuroscience revolution of the past half century. We are finally seeing, in many experimental domains, how subjective psychological processes are related to a demonstrable impact on the objective dynamics of the brain.

The first half dozen chapters of this text attempt to bridge between the clinical and scientific issues. To do this, we have to blend the fine and abundant evidence that is being derived from rather indirect studies of the human brain/mind and the detailed knowledge about brain functions we can cull from our fellow creatures, who also live emotional lives that deserve our close attention and sympathy. These subtle issues, such as the fundamental neural nature of affective experiences, need to be discussed not only in neural terms, but also in terms of the evolved substrates and qualities of consciousness. The logo of this book reflects this philosophy of recognizing that the multiple layers of brain/mind evolution are reflected in the evolutionary passages which serve as a foundation for the human mind.

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# BIOLOGICAL PSYCHIATRY SKETCHED—PAST, PRESENT, AND FUTURE

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## OVERTURE

It is a difficult task to capture the history of biological psychiatry in a brief essay. Let me frame this modest effort in a timeless humanistic perspective.

Psychiatry is the study and treatment of troubled mental lives. Its ultimate goal is to heal broken spirits. At its core, it is an attempt to better understand human thoughts and emotions and to allow this understanding to inform the healing arts. Despite our modern scientific hubris, we know rather little about how brains truly construct our minds and passions. Partly, this is because few scholars have come to terms with the need to understand the evolutionary neural dynamics that affective experiences are ultimately made of. It is all too easy to accept emotions as primitive “givens” and proceed toward a superficial understanding based on words, arbitrary definitions, and the quiddities of logic rather than biology. But the greater and more significant

depths of this mystery have to be plumbed by an integrative neuroscience that has barely emerged.

It is surely not off the mark to claim that the single most important scientific question for biological psychiatry is the accurate decoding of the basic neural nature of affective values and related cognitive experiences. Emotions and moods guide most of our thinking processes and behavioral choices, whether well-arranged or deranged. Many psychopathologies arise from imbalances in these feeling systems that motivate us to think and act in certain ways. At a deep psychological level, that often goes unspoken, emotionally disturbed people have some insight into the weaknesses of their minds. They simply don't know how to manage their persistent psychic disequilibrium. They are certainly no more accustomed to thinking about these psychic forces in neural terms than are the counselors and psychotherapists from whom they seek assistance.

Taxonomic schemes that do not directly acknowledge the underlying emotional faculties of the human mind and brain must be deemed provisional approximations of the goals to which we should aspire. Brain sciences that do not acknowledge or attempt to explore how such processes motivate and guide thinking do no great service to psychiatric thought. Mind sciences that do not dwell on the complexity of the internal world, replete with all manner of feelings and cognitions, do not serve our understanding well. The cognitive, behavioral, and affective sciences must devote equal effort to understanding the embeddedness of mind in brain, body, environment, and culture; otherwise essential components will be overlooked. Only by blending these perspectives judiciously, without inflaming simple-minded polarities such as nurture versus nature, is psychiatric practice well served.

By the end of the 20th century neuroscience had advanced to a point where we now understand the brain rather well. Unfortunately, the discussion of equally important, but more slippery, mind matters continues to lag far behind. Credibly linking facts about the brain to mental functions is maddeningly difficult. There are few incentives in our current system for integrating the abundant peppercorns of brain data into an integrated psychobiological understanding. A prevailing positivistic hope has been that knowledge will emerge automatically from the raw facts like cream rising from freshly expelled milk. To an undesirable degree, theoretical views have been demoted to second-class citizenship. Accordingly, rich discussions of many key functional issues almost disappeared in neuroscience as it mastered how to milk our neural nature during the last third of the 20th century. Indeed, the very concept of productive hypothesizing came to be termed, scornfully, as "mere speculation," perhaps because too many students of the mind (and certainly too many science popularizers) forgot the difference between a "working hypothesis" and a "provisional conclusion." Major textbooks of biological psychiatry and neuropsychiatry no longer discuss emotions prominently. Some consider them needless frills that intervene between reliable diagnostic categories and descriptions of related brain changes. Often, there is little tolerance for such "middle-level" theorizing that seeks to meaningfully link brain functions with mind. One aim of this text is to reverse this trend.