This clinical reference book presents state-of-the-science knowledge about the neurobiology and genetics of the major mental disorders and how this corresponds with their psychiatric features and neuropsychological traits. The text demonstrates how the application of neuropsychology to these disorders provides a more comprehensive foundation for greater accuracy in assessment, diagnosis, and treatment. The book focuses on the neuropathological and pathophysiological basis of the various symptoms, emphasizing the biological basis of each disorder. This approach stresses the importance of looking at the other functional impacts of these manifestations (for example, cognitive deficits secondary to depression).

The text compares adult versus child presentation of psychiatric disorders and covers the major forms of psychopathology including ADHD; Learning Disabilities; Pervasive Developmental Disorders; Mood, Anxiety, Personality, and Schizophrenic Disorders; Cortical and Subcortical Dementias; and Delirium. The book is written for clinical professionals to increase diagnostic accuracy and intervention success and to provide a way to approach psychopathologies as disorders of the neurological system.

Key Features:

- Provides state-of-the-science knowledge about the application of neuropsychological practice to the major forms of psychopathology
- Examines neurological and neuropsychological features of the major forms of psychopathology
- Demonstrates how the application of neurobiology and genetics to psychiatric disorders can increase accuracy of assessment, diagnosis, and treatment
- Considers adult versus child presentation of psychiatric disorders
The Neuropsychology of Psychopathology
Chad A. Noggle, PhD, is an Assistant Professor of Clinical Psychiatry and Chief of the Division of Behavioral and Psychosocial Oncology at Southern Illinois University–School of Medicine. He previously served as an Assistant Professor at both Ball State University and Middle Tennessee State University. Dr. Noggle holds a BA in Psychology from the University of Illinois at Springfield and completed his MA and PhD at Ball State University with specialization in Clinical Neuropsychology. He completed a two-year postdoctoral residency at the Indiana Neuroscience Institute at St. Vincent’s Hospital with specialization in Pediatric and Adult/Geriatric Neuropsychology. To date, Dr. Noggle has published more than 300 articles, book chapters, encyclopedia entries, and research abstracts and has made over 100 presentations at national and international conferences in neuropsychology. He served as the lead editor of The Encyclopedia of Neuropsychological Disorders. He currently serves as a reviewer for a number of neuropsychology journals and is a member of the Editorial Board for Applied Neuropsychology-Adult and Applied Neuropsychology-Child. Dr. Noggle is a member of the American Psychological Association (APA; Divisions 5, 22, 38, 40), the National Academy of Neuropsychology, and the International Neuropsychological Society. He is a licensed psychologist in both Illinois and Indiana. His research interests focus on both adult and pediatric populations, spanning psychiatric illnesses, dementia, PDDs, and neuromedical disorders.

Raymond S. Dean, PhD, ABPP, ABN, holds a BA degree in Psychology (magna cum laude) and an MS degree in Research and Psychometrics from the State University of New York at Albany. As a Parachek-Frazier Research Fellow, he completed a PhD in School/Child Clinical Psychology at Arizona State University in 1978. Dr. Dean completed an internship focused on neuropsychology at the Arizona Neuropsychiatric Hospital and postdoctoral work at the University of Wisconsin at Madison. Since his doctoral degree, he has served in a number of positions and has been recognized for his work. From 1978–1980, Dr. Dean was an Assistant Professor and Director of the Child Clinic at the University of Wisconsin at Madison. During this time, he was awarded the Lightner Witmer Award by the School Psychology Division of the American Psychological Association. From 1980–1981, he served as Assistant Professor of Psychological Services at the University of North Carolina at Chapel Hill. From 1981–1984, Dr. Dean served as Assistant Professor of Medical Psychology and Director of the Neuropsychology Internship at Washington University School of Medicine in St. Louis. During this same time, Dr. Dean received both the Outstanding Contribution Award from the National Academy of Neuropsychology and the Early Contribution Award by Division 15 of the APA. He was named the George and Frances Ball Distinguished Professor of Neuropsychology and Director of the Neuropsychology Laboratory at Ball State University and has served in this position since 1984. In addition, Dr. Dean served as Distinguished Visiting Faculty at the Staff College of the NIMH. Dr. Dean is a Diplomate of the American Board of Professional Psychology, the American Board of Professional Neuropsychology, and the American Board of Pediatric Neuropsychology. He is a Fellow of the APA (Divisions: Clinical, Educational, School and Clinical Neuropsychology), the National Academy of Neuropsychology, and the American Psychopathological Association. Dr. Dean is a past president of the Clinical Neuropsychology Division of the APA and the National Academy of Neuropsychology. He also served as editor of the Archives of Clinical Neuropsychology, Journal of School Psychology, and the Bulletin of the National Academy of Neuropsychology. Dr. Dean has published some 600 research articles, books, chapters, and tests. For his work, he has been recognized by awards from the National Academy of Neuropsychology, the Journal of School Psychology, and the Clinical Neuropsychology Division of the APA.
The Neuropsychology of Psychopathology

EDITORS
Chad A. Noggle, PhD
Raymond S. Dean, PhD, ABPP, ABN
To my wife Jennifer and children, Parker, Carsyn, and Kynedi, with all my love. To my sister for your constant support—CAN

To my children with all my heart—RSD
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Contributors

Daniel N. Allen, PhD
Lincy Professor of Psychology
Department of Psychology
University of Nevada, Las Vegas
Las Vegas, NV

Anjuli R. Amin, PhD
Psychologist
Home Based Primary Care (HBPC) Program
Edward Hines, Jr. VA Medical Center
Hines, IL

James R. Batterson, MD
Child & Adolescent Psychiatrist
Associate Professor of Pediatrics
Children’s Mercy Hospitals and Clinics
University of Missouri–Kansas City SOM
Kansas City, MO

Desiree L. Bindus
Howard University
Washington, DC

Leslie H. Brown
Postdoctoral Fellow
Department of Psychiatry
University of Pittsburgh
Pittsburgh, PA

Deborah Ely Budding, PhD
Clinical Neuropsychologist
Private Practice
Manhattan Beach, CA

Gina Cancelliere
Philadelphia College of Osteopathic Medicine
Philadelphia, PA

Catherine Cook-Cottone, PhD
Associate Professor
Department of Counseling, School, and Educational Psychology
The University at Buffalo, SUNY
Buffalo, NY

Jeremy J. Davis, PsyD
Clinical Neuropsychologist
Assistant Professor (Clinical)
Division of Physical Medicine & Rehabilitation
University of Utah School of Medicine
Salt Lake City, UT

Raymond S. Dean, PhD, ABPP, ABN
George & Frances Ball Distinguished Professor of Neuropsychology
Director, BSU Neuropsychology Laboratory
Professor of Psychology
Director of Educational Psychology
Department of Educational Psychology
Ball State University
Muncie, IN

Esther Direnfeld
Graduate Student
Department of Psychology
University of Victoria
Victoria, British Columbia, Canada

Jeff Frazer
Graduate Student
Department of Psychology
University of Victoria
Victoria, British Columbia, Canada
CONTRIBUTORS

Mauricio A. Garcia-Barrera, PhD  
Assistant Professor  
Department of Psychology  
University of Victoria  
Victoria, British Columbia, Canada

Emily Gilmore, PsyD  
Department of Extended Care and Rehabilitation  
VA Northern Indiana Health Care System  
Marion, IN

Jodene Goldenring Fine, PhD  
Assistant Professor  
Department of Counseling, Educational Psychology, and Special Education  
Michigan State University  
East Lansing, MI

Gerald Goldstein, PhD  
Senior Research Career Scientist  
Mental Illness Research, Educational and Clinical Center  
VA Pittsburgh Healthcare System  
Pittsburgh, PA  
and  
Clinical Professor of Psychiatry  
Department of Psychiatry  
University of Pittsburgh  
Pittsburgh, PA

Stéphane Guay, PhD  
Associate Professor  
School of Criminology  
University of Montréal  
Montréal, Québec, Canada

Gretchen L. Haas, PhD  
Director  
VA Mental Illness Research, Educational and Clinical Center  
VA Pittsburgh Healthcare System  
Pittsburgh, PA

Lisa A. Hain, PsyD, ABSNP  
Assistant Professor  
Department of Psychology  
Philadelphia College of Osteopathic Medicine  
Philadelphia, PA

Mary E. Haines, PhD, ABPP  
Clinical Neuropsychologist  
Clinical Associate Professor  
Departments of Physical Medicine and Rehabilitation and Psychiatry  
University of Toledo Medical Center  
Toledo, OH

James B. Hale, PhD  
Professor, Faculties of Education and Pediatrics  
Department of School and Applied Child Psychology  
University of Calgary  
Calgary, Alberta, Canada

John Joshua Hall, PhD  
Clinical Neuropsychologist  
Assistant Professor  
Department of Pediatrics  
Children’s Mercy Hospitals and Clinics  
University of Missouri–Kansas City SOM  
Kansas City, MO

Margie Hernandez  
Graduate Student  
Department of Psychology  
University of North Carolina–Wilmington  
Wilmington, NC

Javan Horwitz, PsyD  
Clinical Neuropsychologist  
Department of Extended Care and Rehabilitation  
VA Northern Indiana Health Care System  
Marion, IN

Natalie Horwitz, MA  
Carmel Neuropsychology Services, P.C.  
Carmel, IN

Rhonda Johnson, PhD  
Associate Professor  
Department of Psychiatry & Behavioral Sciences  
Department of Medical Oncology  
The University of Kansas School of Medicine  
Westwood, KS

Leonard F. Koziol, PhD  
Clinical Neuropsychologist  
Private Practice  
Arlington Heights, IL

Morten L. Kringelbach, PhD  
Senior Research Fellow  
Department of Psychiatry  
University of Oxford, Oxford, UK  
and  
Professor of Neuroscience  
Centre for Functionally Integrative Neuroscience (CFIN)  
University of Aarhus, Aarhus, Denmark
Margaret Semrud-Clikeman, PhD  
Professor of Pediatrics  
Division Director of Clinical Behavioral Neuroscience  
University of Minnesota Medical School  
Minneapolis, MN

Amanda Smith, MS  
Associate Professor  
Department of Counseling, School, and Educational Psychology  
The University at Buffalo, SUNY  
Buffalo, NY

Jeffrey H. Snow, PhD  
Associate Professor  
University of Arkansas for Medical Sciences  
Little Rock, AR

Stephen Soltys, MD  
Professor and Chairman  
Department of Psychiatry  
Southern Illinois University–School of Medicine  
Springfield, IL

Gerry A. Stefanatos, DPhil  
Chairman, Department of Communication Science and Disorders  
Temple University  
Philadelphia, PA

Melissa M. Swanson, PhD  
Neuropsychology Fellow  
Department of Physical Medicine and Rehabilitation  
University of Toledo Medical Center  
Toledo, OH

Anthony Swentosky, PhD  
School Psychologist  
Harrison School District 2  
Colorado Springs, CO

Nicholas S. Thaler  
Graduate Student  
Department of Psychology  
University of Nevada, Las Vegas  
Las Vegas, NV

Chrisceelyn Tussey, PsyD  
Director of Psychological Assessment  
Bellevue Hospital Center  
New York, NY  
and  
Clinical Assistant Professor  
Department of Psychiatry  
New York University School of Medicine  
New York, NY

Jacqueline Remondet Wall, PhD, CRC  
Associate Professor  
School of Psychological Sciences  
University of Indianapolis  
Indianapolis, IN

Douglas Watt, PhD  
Clinical Neuropsychologist  
Cambridge Health Alliance  
Harvard Medical School  
Boston, MA  
and  
Clinic for Cognitive Disorders  
Quincy Medical Center  
Boston University School of Medicine  
Boston, MA

Lisa L. Weyandt, PhD  
Department of Psychology  
University of Rhode Island  
Kingston, RI

John M. Wryobeck, PhD, ABPP  
Associate Professor  
Department of Psychiatry  
University of Toledo College of Medicine  
Toledo, OH

Timothy F. Wynkoop, PhD  
Clinical Forensic Neuropsychologist  
Private Practice  
Maumee, OH  
and  
Clinical Assistant Professor of Psychiatry  
Faculty, UTMC Clinical Neuropsychology Fellowship Program  
University of Toledo College of Medicine  
Toledo, OH

K. S. Young  
Department of Psychiatry  
Warneford Hospital  
University of Oxford, Oxford, UK  
and  
Centre for Functionally Integrative Neuroscience (CFIN)  
University of Aarhus, Aarhus, Denmark

Davor N. Zink, MA  
Graduate Student  
Department of Psychology  
University of North Carolina–Wilmington  
Wilmington, NC
Motivation, behavior, and emotions are by-products of brain activity. This serves as the foundation upon which modern shifts in the clinical neurosciences have been built. However, the centrality of neurobiology in human behavior is not intended to diminish the role the environment plays in such features. Rather, it serves to emphasize that the individual’s neurological makeup mediates his or her interaction with the environment and the effect environmental experiences have on neurobehavioral outcomes. The clinical neurosciences, including neuropsychology, neuropsychiatry, and behavioral neurology, are disciplines focused on understanding the neurobiological correlates of behavior. In addition, these specialties are focused on the assessment, identification, and treatment of dysfunctional behavior and disorders.

With advances across the neurosciences, our understanding of behavior and neuropsychiatric disorders has grown by leaps and bounds. Since the earliest of times, humankind has been interested in behavior and its roots. Psychiatric presentations have received particular attention historically. Proposals as to the origin of these manifestations has shifted from beliefs in the role of evil spirits to our current understanding of the role neurophysiology plays in the development of these various disorders. Sizeable shifts have been seen even in the field of neuropsychology. In the past, neuropsychologists in the psychiatric setting were asked to differentiate “organic” and “functional” mental disorders because the two were viewed as mutually exclusive. This conceptualization is now recognized as flawed.

The integration of neuroscience, neuropsychology, and traditional psychiatric practices has refined our understanding of those presentations outlined by the DSM-IV-TR and the proposed DSM-5—presentations that have historically been termed psychopathologies. Studies in structural and functional imaging, genetic analysis, and molecular biology have expanded our knowledge of the biological basis of such behavior and disorders. The emergence of this literature has shifted not only our knowledge base, but also the nomenclature we utilize. Those behaviors and disorders traditionally falling under the psychopathology heading are now better defined as neuropsychiatric disorders.

Neuropsychology is a unique discipline within the clinical neurosciences because it integrates neuroscience and clinical and cognitive psychologies. When it comes to neuropsychiatric disorders, looking through a neuropsychological lens allows us to conceptualize such manifestations not simply by their behavioral features, but also their cognitive and neurobehavioral traits. In the current book, The Neuropsychology of Psychopathology, neuropsychiatric features and disorders are discussed from both a neuroscientific and neuropsychological perspective. Chapters cover both the neurobiological and neurocognitive correlates of common psychiatric presentations such as major depression, bipolar disorder, posttraumatic stress disorder (PTSD), and schizophrenia, among others. Additional presentations included within the DSM-IV-TR are discussed including Alzheimer’s disease, perva-
sive developmental disorders, learning disabilities, and delirium, as well as others. Founda-
tional concepts are also discussed, including discussion of the neuroanatomy of pleasure
and emotion as well as neurological differences between children and adults that lead to
discrepancies in the appearance of clinical manifestations. Clinical-based applications are
also discussed, including the role of neuropsychology within the psychiatric setting, the
utility of psychological assessment, and the neurobiological basis of psychotherapy.
We would like to acknowledge the work put forth by the assistant editors for this book, including Dr. John Joshua Hall, who served as Lead Assistant Editor, Dr. Michelle Pagoria, Dr. Amy R. Steiner, and Dr. Javan Horwitz.

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SERIES EDITORS
Chad A. Noggle, PhD
Raymond S. Dean, PhD, ABPP, ABN

The Neuropsychology of Psychopathology
The Neuropsychology of Cancer and Oncology
Neuropsychological Rehabilitation
The Neuropsychology of Cortical Dementias
The Neuropsychology of Pervasive Developmental Disorders
The Neuropsychology of Psychopharmacology
Principles of Psychopathology
CHAPTER 1

The Neuropsychology of Psychopathology: Historical Shifts

Anjuli R. Amin & Chad A. Noggle

INTRODUCTION

The field of psychology has emerged from a mix of social, political, scientific, and philosophical sources. Throughout time, individuals from a variety of disciplines and across the world’s cultures have made attempts to understand our diverse mental and behavioral processes. From mere speculation to actual hands-on experimentation, efforts to learn more about what motivates certain behaviors, the causes of psychopathology, and the methods of treating psychological illnesses have emerged from a wide range of sources.

At the very core of psychology as a discipline lie efforts to explain those behaviors that have been perceived as abnormal. The conceptualization of what behavior is considered out of the norm has changed over time, including how we define and explain such behavior. Over time there has been a movement from supernatural and religious considerations of psychopathology to a paradigm that has integrated biological and environmental variables. The most recent developments in the area of psychopathology, beginning in the 19th century, have consisted of an integration of various psychological theories and models with consistent advances in scientific thought and inquiry. Such changes in the field have led us to a contemporary approach to psychopathology that combines multiple elements.

HISTORICAL VIEWS OF PSYCHOPATHOLOGY

Ancient Times

Evidence of psychological thought, beyond the musings of Plato and Aristotle, have been found within many ancient cultures. Even though psychopathology did not emerge as a significant area of scientific interest until the late 19th century, speculation about the origin, causes, and functions of abnormal behavior has been traced as far back as the 16th century B.C. to the ancient Egyptians. Among the ancient Egyptians, concepts related to health emerged from a mix of scientific and religious perspectives. A commonly held belief was that most mental functions emanated from the heart (Viney & King, 2003). The brain, although noted to play a role in speech and memory disorders, was thought to be subservient to this vital organ and unimportant in comparison (Rains, 2002). The heart was perceived to embody an array of cognitive processes that included memory, wisdom, emotion, and intelligence. The importance of the heart was further emphasized in Egyptian spiritual beliefs, wherein
one’s heart was considered the key to being granted access to the afterlife. The Egyptians carried these beliefs, which they incorporated with empirical observation, into developing an integrated approach to medicine. They emphasized the importance of maintaining a balance in the soul and built special temples for the mentally ill, incorporating spiritual aspects into the treatment of emotional disorders. Factors such as insects, filth, and the devil were often viewed as causes of psychopathology, and these illnesses were often treated using a broad range of therapies (e.g., rituals, surgery, enemas, incantations, and medications; Viney & King, 2003).

Spirituality and religion were also integrated into discourses on psychology and human behavior within the region now known as India and Pakistan around 800 B.C. Many of these thoughts were found within the *Upanishads* (Brennan, 2002). Considered one of the oldest sacred scriptures of the Hindu religion, the *Upanishads* consisted of over 1,000 lectures given by various scholars. Included within these discourses were philosophical and spiritual notions about a person’s relationship to the universe. In contrast to contemporary Western ideas of what constituted healthy psychological development (i.e., an emphasis on autonomy and independence), the views expressed in the *Upanishads* portrayed acts of individualism as wayward. Importance was placed on an individual’s place within and connection to a larger, more valued entity—the universe. An emphasis on communalism and maintaining harmony within society was thus reflected in psychological thought at the time. For example, it was thought that mental disorders could result from an unwarranted amount of emotional expression and that one’s personality traits could be traced back to characteristics displayed by the mother during pregnancy (Viney & King, 2003). It was common to believe that having an ill temper during pregnancy would result in giving birth to a child with some type of disorder, such as epilepsy. Thus, the value of an individual’s relationship to her or his environment was reflected in societal ideas of acceptable human behavior at the time. Actions that appeared to be individualistic in nature were thought to be of harm to or in disfavor of one’s community.

A strong emphasis on religious explanations of psychological disorders remained prevalent in the area of Persia. Around the 6th century B.C., and during the time of the birth of the Zoroastrian religion, emotional disorders were often viewed as being caused by the devil (Viney & King, 2003). Treatment of psychological issues thus consisted of religious practices such as exorcism, incantations, and magical rites. The integration of philosophy and science was not openly welcomed within Persian society, and thus a strong focus on religion within the field of health was sustained (Viney & King, 2003).

Views integrating empirical-rational and magical-religious perspectives about psychopathology were observed around 200 B.C. in early Chinese culture. Psychological thought during this time was influenced by the principles of yin and yang—two opposing forces that represented all universal opposites (e.g., softness/hardness, cold/heat, or creation/completion; Liu, 2006). Both yin and yang were used to explain different phenomena, including human behavior. Specifically, it was believed that maintaining a balance between these two forces was essential to ensuring one’s physical and psychological well-being. At this time, it was also perceived that all mental processes were fostered within the physical structures of the body, opening the door to a physiological psychology that placed equal importance on mind and body components (Viney & King, 2003).

**Hippocrates’s and Galen’s Contributions**

What is known thus far regarding conceptualizations of psychopathology from ancient perspectives is that often a supernatural explanation was attached to an observed mental disorder (Chamorro-Premuzic, 2007). Treatment of such disorders also consisted of similar methodologies, which included exorcisms, shamanism, and other spiritual interventions. A significant change in the trajectory of thought concerning human nature appeared during the period of 600–400 B.C. This shift in thought emerged from the early Greek philosophers, who began to view the world in terms of natural explanations, emphasizing that things in the universe were controlled by natural principles and not “the whims of the gods” (Hergenhahn, 2005, p. 28).
Although much focus was placed on the heart, brain–behavior relationships began to emerge around this time. Archeologists have discovered several thousand skulls from this time period that show evidence of humans having survived trephination (Zillmer & Spiers, 2001). Trephination is the ancient practice of removing pieces of the skull to relieve swelling of the brain. Some believe the procedure was intended to allow the evil spirits that were plaguing the individual, and contributing to his or her psychological dysfunction, to escape. The ancient Greeks produced the first written records of brain–behavior relationships, although they still regarded cognitive functioning as arising from a divine nature. The first recorded observation that proposed the brain as the center of human reasoning was produced by Pythagoras (580–500 B.C.). Pythagoras and other scholars developed the idea of the brain hypothesis, which stipulated that the brain is the source of all behavior (Zillmer & Spiers, 2001).

Hippocrates (460–377 B.C.), who is commonly regarded as the father of modern Western medicine, was among the first to suggest that psychological disorders could be treated no differently than other “physical” diseases. As scribed in the Hippocratic Corpus (Maher & Maher, 1994), Hippocrates went as far as to hypothesize that these psychological “diseases” arose from the brain, which he had long held to be the site of wisdom, consciousness, intelligence, and emotion. Over the next 600 years, although followers of Hippocrates’s works maintained the belief of the brain being the origin of psychological disorders, spiritual/religious theory remained dominant. Truly, the extent of Hippocrates’s brilliance when taking into consideration time, place, resources, and prior knowledge was not fully appreciated until modern times.

Around the same time of Hippocrates, Plato (420–347 B.C.) began to propose his theories of the mind and soul. Plato wrote that the soul, responsible for rational thought, was located in the brain and noted, secondary to case studies, that head trauma can result in impairment in reasoning (Robinson, 1970). Aristotle (384–322 B.C.), though a student of Plato, disagreed with Plato’s localization of mental processes. He instead postulated that the heart was the seat of all mental processes and emotions. Plato felt the brain’s involvement in cognition and emotion was to regulate the actions of the heart, a viewpoint that came to be known as the cardiac hypothesis (Zillmer & Spiers, 2001). Though he made numerous contributions to ethics, psychology, poetry, and politics, Plato’s viewpoint of the location of the soul led to a regression in the understanding of brain–behavior relationships. The ideas of the Greek philosophers, although anatomically wrong in many counts, provided the foundation upon which the study of neuropsychology was built, and future philosophers and physiologists may not have made their contributions without the advances of the Greeks.

Galen (129–198 A.D.), a follower of Hippocrates’s writings, expanded his theories of the mind and origin of psychological disorders. Most notably, Galen expanded Hippocrates’s Humoral Theory of Disorders. This Hippocratic-Galenic theory suggested normal functioning along cognitive, emotional, behavioral, and spiritual lines was dependent on a homeostasis, or balance, of four influential body fluids (i.e., blood, black bile, yellow bile, and phlegm). Hippocrates initially proposed that significant elevations or depletions of any of these fluids disrupted the homeostasis of the system and led to an “imbalance” of the person, thereby bringing about disordered behavior. He further proposed that the nature of the fluid imbalance corresponded with the specific behavioral constellation, and that by observing the dysfunctional behavior one may determine which fluids were elevated or depleted. Although we do not discuss “bile” in our modern day conceptualization of psychiatric disorders or functional domains, if one were to replace “humors” with neurotransmitters, it is easy to see the prominent overlap of Hippocrates’s and Galen’s theories with modern-day knowledge and thus appreciate their insight. Consequently, therapies were developed to “restore” balance of these fluid levels. Bloodletting, induced vomiting, and even manipulation of body temperature were methods employed to rebalance the different humors.

Beyond expansion of Hippocrates’s work, Galen’s unique contributions came in his description of the anatomy of the nervous system. Through combining his anatomical findings with behavioral observations, Galen proposed that causes of psychological disorders could be divided into physical and mental categories including head injuries, shock, fear, alcoholism, menstrual changes, economic trouble, and heartbreak (Butcher, Mineka, & Hooley, 2008, p.
12). His observations of the human body came from his work as a surgeon who was appointed to the care of gladiators (Finger, 1994a). Little elaboration was made over the next thousand years because Galen’s view of humors became so ingrained. His expansions of Hippocrates’s theories remained prominent until the 16th century, when his anatomic mistakes began to be corrected.

The Middle Ages

The Middle Ages saw a growth in the science of medicine within the Middle East. Baghdad became home to the first mental hospital in 792 A.D., with two more established soon after, in Damascus and Aleppo, (Polvan, 1969). It was at this time that Avicenna (980–1037 A.D.), a physician from Arabia, was recognized as the most highly touted physician. He often wrote of hysteria, epilepsy, manic reactions, and melancholia and discussed the benefit of humane treatment of patients. Still, rituals and superstition remained the most prominent treatment pursuits, particularly in Europe, where the treatment of patients was even far less humane. Scientific investigations were not readily undertaken as conceptualizations of psychiatric disorders reverted back to spiritual explanations and demonology. Consequently, clergy served as the primary care providers for mentally ill individuals. Treatment involved prayer, holy water, sanctified ointments, the breath or spittle of the priests, the touching of relics, visits to holy places, and mild forms of exorcism (Butcher et al., 2008, p. 13). Although many have long discussed the thought or concept of witchcraft in the Middle Ages as being a case of misdiagnosed mental illness, some have called this into question (Maher & Maher, 1985). In reality, those accused of witchcraft tended to be disheveled-looking, single women with a bad temper who tended to talk back to others or exhibit a “sharp tongue” (Schoeneman, 1984).

Challenges to the Church

Paracelsus (1490–1541) was recognized as a key opponent to the superstitious belief of mental illness. He suggested that various psychiatric presentations were not manifestations of possessions but by-products of physical disease. Paracelsus did, however, believe in the effects of astrology, the moon in particular. He felt the brain was directly affected by the moon and its phases (Mora, 1967).

Johann Weyer (1515–1588) was a German physician who shared the belief during this time period that mental illness was physically based. Weyer was particularly troubled by the way in which people with mental illnesses were treated, largely because of the spiritual beliefs of those around them. At this time, however, his views were seen as contradicting the Church itself. Consequently, Weyer was persecuted by those around him for his hypotheses.

St. Vincent de Paul (1576–1660) was another individual who stood against the suggestion of mental illness being a manifestation of possession or witchcraft. His stance was particularly important because he represented the first individual within the Church itself to take such a stance. St. Vincent de Paul proposed that psychiatric disorders were no different from bodily diseases and the Church should protect these individuals and aid in relieving their symptoms as opposed to persecuting them.

MODERN SHIFTS IN THE NEUROBIOLOGY OF PSYCHOPATHOLOGY

Although the theories of Hippocrates and Galen persisted on, historical review demonstrates they fell in and out of favor as different thoughts and concepts emerged throughout the centuries. It was not until the 19th century that interest in the biological basis of psychological disorders was again sparked. Interestingly, this was not brought about by an influential scientist or emerging scientific findings from controlled research studies; rather, it was stirred by the discovery of syphilis and its treatment. Practitioners charged with the care of those with psychosis noted over time that a subgroup of patients demonstrated a fairly steady
deterioration in physical status, eventually leading to paralysis and death within approximately 5 years of symptom onset. This contrasted the pattern exhibited by other psychotic patients. The etiology of this subgroup was eventually termed general paresis. Through the work of Louis Pasteur and others, the bacterial organism that caused syphilis and syphilis’s link with general paresis was eventually discovered. Autopsies demonstrated the invasion of brain tissue as the potential basis for the behavioral changes. Consequently, science and medicine had a clear example of how invasion of the brain by the bacteria involved in syphilis brought about psychological change, thereby suggesting other psychological disorders may also arise from the brain itself. When penicillin was eventually developed and demonstrated the capacity to ward off the neuropsychiatric sequelae of syphilis, it led many to question if other psychiatric features may also respond to biologically based treatments.

It was also during the 19th century that John Grey came into prominence as a leading figure in the biological movement. Much of his influence was seen through his work in the state hospital of New York. Grey firmly believed that psychiatric disorders were always of a physical origin. As such, patients were treated within the hospital as though they were physically ill, with patients getting rest, having a properly managed diet, having access to natural light, having clear and ventilated air, and having regulated room temperature. Just by making these environmental changes, improvements were seen. As patients did better physically, they also did better mentally. Consequently, these anecdotal findings reinforced for Grey that these disorders were physically based while also demonstrating the relative contribution of environmental factors. Around this same time, Emil Kraepelin (1856–1926) was instrumental in the refinement of the diagnosis and classification of psychiatric disorders. He described the concept of different psychiatric disorders, with different origins and times of onset, which he likened to different biological factors.

The revitalization of the neurobiological basis of psychiatric disorders came at the same time that our understanding of the brain’s role in other functional domains was increasing through case studies and scientific investigation. Emanuel Swedenborg (1688–1772) was one of the first to generate a theory of cortical localization of behavioral functions. Swedenborg wrote that separate areas of the brain were necessary to prevent psychological chaos, and charted his ideas of discrete areas for vision and hearing based on his studies of pathology and anatomy (Finger, 1994b).

Paul Broca (1824–1880) is one of the most recognized figures of the localization movement, identifying specific functional areas within the cerebrum. He is best remembered for identifying an area of the brain that we now call Broca’s area that is related to expressive speech.

Carl Wernicke (1848–1904), another 19th century researcher, postulated that the ability to understand spoken language had a specific localization site in the brain, in the posterior half of the left superior temporal gyrus. Wernicke was also responsible for casting light on a disorder that may have been previously referred to as madness in earlier centuries, which was actually a problem of the left hemisphere (Harris, 1999). Wernicke’s findings are important in brain localization theory because, along with Broca, he was able to demonstrate that language is located in at least two different cortical areas. Wernicke’s findings cast a realistic shadow on 19th century proponents of brain localization theory who hypothesized functions had one specific location. At the same time, it provided a general support for the movement toward the brain being the center of functioning.

When it comes to personality, emotions, and behaviors specifically, the case of Phineas Gage, a railroad worker who suffered a traumatic brain injury when an explosion forced a large piece of metal into the front of his brain, serves as the most common case example. Although he recovered with his lower order functions (respiration, heart rate) intact, he suffered a noticeable change in personality and behavior. This and other cases of people surviving injuries led to speculation that elements of personality could be localized in the frontal lobes.

Biological Interventions

Renewed focus on the biological basis of psychiatric disorders brought about increased use of biologically focused interventions. In 1927, Manfred Sakel stumbled across what would
come to be known as insulin shock therapy. Sakel, in trying to stimulate eating in psychotic patients, began to administer increasing amounts of insulin. He observed that once patients were given a certain amount, they would actually begin to convulse and eventually go comatose for a period of time (Sakel, 1958). As patients regained their faculties, Sakel and his colleagues noticed that some of the patients actually exhibited improvement in their mood and psychiatric status. Sakel suggested the convulsion was the source of the psychiatric improvement. However, insulin shock therapy never became widely used because there was significant risk for prolonged coma or even death. Still, insulin shock therapy led the way for electroconvulsive therapy (ECT) to be considered.

In fact, the potential benefits of ECT were proposed over 150 years earlier when Benjamin Franklin and a friend of his not only noted that a moderate electrical shock to the brain was safe, even though it caused a convulsion and brief amnesia, but that it also was accompanied by an improvement in mood, which Franklin’s friend described as a “strange elation” (Finger & Zaromb, 2006, p. 245). In 1938, a depressed patient was successfully treated with ECT based on the suggestions of Ugo Cerletti and Lucio Bini, two Italian surgeons (Hunt, 1980). The methods used have been modified, but ECT remains a treatment used today.

The 1950s saw the development of psychotropic agents for severe psychotic disorders. Developers sought to offer chemical control of the psychiatric features while maintaining the greatest degree of functionality on the part of the patient. Prior to these newer agents, the chemicals used were primarily sedating. They offered a chemical restraint of individuals as opposed to physical restraint. Although this made patients easier to handle by staff in psychiatric institutions, patients had no real life or time for social interaction because of the sedating effects. Neuroleptics and benzodiazepines initially came into favor at this time, but they too were eventually linked with negative side effects. Their use continued to grow well into the 1970s.

**CURRENT TRENDS AND MOVEMENTS**

Contemporary technologies have offered great insight into the biological correlates of the various psychological disorders. Convergence of advances in neuroimaging, molecular genetics, and endocrinology has elucidated the nature of psychopathology. The combination of these scientific pursuits has provided valuable information attesting to the dependence of mental functioning on brain processes and to the mechanisms underlying various forms of psychopathology (Meissner, 2006). The end result is that the neurophysiology of many mental disorders is being increasingly and rapidly clarified and specified. As such, specific psychological-behavioral deficits can be directly or indirectly connected to brain dysfunction, yet there is a range of individual variation in the details of psychological impairment associated with otherwise identical lesions (Meissner, 2006).

The incorporation of neuropsychology within the scientific evaluation of psychiatric disorders emerged over the past few decades as a need emerged to use the theoretical models from normal cognitive psychology to understand psychiatric symptoms in a principled and testable manner (Halligan & David, 2001). As a result, psychiatric features are slowly coming to be understood in terms of disturbances to recognized information-processing systems (Halligan & David, 2001).

**SUMMARY**

The etiology of psychopathologies has seen many proposals over the centuries. Records show our concepts on the subject have shifted from a religious/spiritual mindset to a multidimensional model where biological and environmental factors interact to form the basis of the various psychiatric presentations. With advances in neuroimaging, genetics, and functional assessment, we find ourselves at a point when our understanding of the psychopathologies is growing by leaps and bounds. The following chapters will discuss what we now know of the neurobiology and genetics of the various recognized psychiatric disorders, how this
corresponds with their psychiatric features and neuropsychological traits, and how this knowledge allows for refined diagnostics and treatment. In other words, the chapters to come will discuss The Neuropsychology of Psychopathology. This knowledge can be used to expand one’s clinical skills and knowledge to better serve the patient populations discussed within this text because a neuropsychological formulation offers the most comprehensive view of the impact of these disorders on everyday functioning. Not to know this information is to attempt to treat those manifestations without a grasp of all the contributing factors.

REFERENCES
