Adult Psychopathology and Diagnosis

SEVENTH EDITION

Edited by

Deborah C. Beidel B. Christopher Frueh Michel Hersen

WILEY

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and Michel Hersen

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Preface

This is the seventh edition of *Adult Psychopathology and Diagnosis* and the second that does not bear Samuel M. Turner's name due to his untimely passing. His spirit is here, however, and we again dedicate this volume to him.

Since publication of the previous edition, the *DSM-5* has been released and new data continue to emerge that force us to continuously reconsider how we approach and conceptualize psychological disorders. Psychopathology is a vibrant field and continuing discoveries regarding the roles of genetics, neurobiology, and behavior require that we continue to update this volume for students and professionals alike. We believe that our eminent authors have captured both major changes and more nuanced findings in their respective chapters.

The seventh edition contains 20 chapters divided into two parts (Part I: Overview; Part II: Specific Disorders). Part I has four chapters by experts in the field: Chapter 1: Mental Disorders as Discrete Clinical Conditions: Dimensional Versus Categorical Classification; Chapter 2: The Problem of Dual Diagnosis; Chapter 3: Structured and Semistructured Interviews for Differential Diagnosis: Fundamentals, Applications, and Features; and Chapter 4: Impact of Race, Ethnicity, and Culture on the Expression and Assessment of Psychopathology.

Part II on Specific Disorders includes 16 chapters that cover many of the diagnostic entities and problems seen in daily clinical work by our colleagues in hospitals, clinics, and private practice. Approximately 30% of the chapters have new authors for this edition. Additionally, as a testament to the vibrancy of the field of psychopathology, the original anxiety disorders chapter has now been split into three chapters (Chapter 8: Panic Disorder, Agoraphobia, Generalized Anxiety Disorder, Social Anxiety Disorder, and Specific Phobias; Chapter 9: Obsessive-Compulsive and Related Disorders; and Chapter 10: Trauma and Stress-Related Disorders: Posttraumatic Stress Disorder, Acute Stress Disorder, and Adjustment Disorders) in order to adequately address the extensive work in these areas and changes in *DSM-5*.

To the extent possible, we have asked our gracious contributors to follow a standard format. Exceptions, of course, were granted as dictated by the data inherent in each chapter. Generally, however, each chapter has a description of the disorder, a case study, and material documenting epidemiology, clinical picture, course and prognosis, diagnostic considerations, psychological and biological assessment, and etiological considerations. Each chapter also contains a summary.

Many individuals have contributed to the seventh edition of this book. First, we thank our experts, who agreed to share their vast knowledge about their areas of

study. And as always, we thank Patricia Rossi and her exceptionally professional staff at John Wiley & Sons, for understanding the importance of this area in clinical psychology.

Deborah C. Beidel, Orlando, Florida
B. Christopher Frueh, Hilo, Hawaii
Michel Hersen, Hillsboro, Oregon

Contributors

Michelle Accardi
Department of Psychology
Binghamton University (SUNY)
Binghamton, NY

Candice A. Alfano, PhD
Department of Psychology
University of Houston
Houston, TX

Gordon J. G. Asmundson, PhD
Department of Psychology
University of Regina
Regina, Saskatchewan, Canada

Evelyn Behar, PhD
Department of Psychology
University of Illinois
at Chicago
Chicago, IL

Melanie E. Bennett, PhD
Department of Psychiatry
University of Maryland,
School of Medicine
Baltimore, MD

Joanna Berg
Department of Psychology
Emory University
Atlanta, GA

Lori A. Brotto, PhD
Department of Obstetrics and
Gynecology
University of British Columbia
Vancouver, BC, Canada

Cynthia M. Bulik, PhD
Department of Psychiatry and
Department of Nutrition
University of North Carolina at Chapel Hill
Chapel Hill, NC

L. Kevin Chapman
Center for Mental Health Disparities
Department of Psychology
University of Louisville
Louisville, KY

Colleen Cleere
Department of Psychology
Binghamton University (SUNY)
Binghamton, NY

Matthew Cohen
Department of Psychology
University of North Carolina at Chapel Hill
Chapel Hill, NC

Dennis R. Combs, PhD
Department of Psychology
University of Texas at Tyler
Tyler, TX

Daniel J. Conybeare
Department of Psychology
University of Illinois at Chicago
Chicago, IL

Stacey B. Daughters, PhD
Department of Psychology
University of North Carolina
at Chapel Hill
Chapel Hill, NC

Ryan C. T. DeLapp
Center for Mental Health Disparities
Department of Psychology
University of Louisville
Louisville, KY

Emily Drake
Department of Psychology
University of Texas at Tyler
Tyler, TX

Leilani Feliciano, PhD
Department of Psychology
University of Colorado at Colorado Springs
Colorado Springs, CO

Thomas A. Fergus
Department of Psychology
Northern Illinois University
Dekalb, IL

Timo Giesbrecht, PhD
Department of Experimental Psychology
University of Maastricht
Maastricht, The Netherlands

Selvija Gjonbalaj-Marovic, PhD
Department of Psychiatry
University of Maryland, School of Medicine
College Park, MD

Gerald Goldstein, PhD
Psychological Service
Veterans Affairs Medical Center
Pittsburgh, PA

Whitney L. Gore
Department of Psychology
University of Kentucky
Lexington, KY

Anouk L. Grubaugh, PhD
Department of Psychiatry
Medical University of South Carolina
Charleston, SC

Christopher J. Hopwood, PhD
Department of Psychology
Michigan State University
East Lansing, MI

Michelle M. Hospital, PhD
Department of Psychology
Florida International University
Miami, FL

Sheri L. Johnson, PhD
Department of Psychology
University of California, Berkeley
Berkeley, CA

Susan C. Kleiman
Department of Psychiatry and Department of Nutrition
University of North Carolina at Chapel Hill
Chapel Hill, NC

Carolin Klein, PhD
Department of Obstetrics and Gynecology
University of British Columbia
Vancouver, BC, Canada

Simon Lau
Department of Psychology
University of Houston
Houston, TX

Anne A. Lawrence, MD, PhD
Department of Psychology
University of Lethbridge
Lethbridge, Alberta, Canada

Scott Lilienfeld, PhD
Department of Psychology
Emory University
Atlanta, GA

Steven Jay Lynn, PhD
Department of Psychology
Binghamton University (SUNY)
Binghamton, NY

Suzanne E. Mazzeo, PhD
Department of Psychology
Virginia Commonwealth University
Richmond, VA

Harald Merckelbach, PhD
Department of Experimental Clinical Psychology
University of Maastricht
Maastricht, The Netherlands

David J. Miklowitz, PhD
Department of Psychiatry–Semel Institute
University of California, Los Angeles
Los Angeles, CA

Kim T. Mueser, PhD
Department of Psychiatry and Community and Family Medicine
Dartmouth College Medical School
Hanover, NH

Sandra M. Neer, PhD
Department of Psychology
University of Central Florida
Orlando, FL

Daniel L. Peluso
Department of Psychology
University of Regina
Regina, Saskatchewan, Canada

Jason Peer, PhD
Department of Psychiatry
University of Maryland School of Medicine
Baltimore, MD

Katie Ragsdale
Department of Psychology
University of Central Florida
Orlando, FL

Brenna N. Renn
Department of Psychology
University of Colorado at Colorado Springs
Colorado Springs, CO

Daniel L. Segal, PhD
Department of Psychology
University of Colorado at Colorado Springs
Colorado Springs, CO

Mark B. Sobell, PhD
Center for Psychological Studies
Nova Southeastern University
Fort Lauderdale, FL

Linda C. Sobell, PhD
Center for Psychological Studies
Nova Southeastern University
Fort Lauderdale, FL

Michel A. Thibodeau
Department of Psychology
University of Regina
Regina, Saskatchewan, Canada

Katherine M. Thomas
Department of Psychology
Michigan State University
East Lansing, MI

Sara E. Trace, PhD
Department of Psychiatry
University of North Carolina at Chapel Hill
Chapel Hill, NC

David P. Valentiner, PhD
Department of Psychology
Northern Illinois University
Dekalb, IL

Eric F. Wagner, PhD
College of Public Health and Social Work
Florida International University
Miami, FL

Thomas A. Widiger, PhD
Department of Psychology
University of Kentucky
Lexington, KY

Kadija N. Williams
Department of Psychology
University of Colorado at Colorado Springs
Colorado Springs, CO

Monnica T. Williams
Center for Mental Health Disparities
Department of Psychology
University of Louisville
Louisville, KY

Kenneth J. Zucker, PhD
Department of Psychiatry and Psychology
University of Toronto
Toronto, Ontario, Canada

PART I

OVERVIEW

CHAPTER 1

Mental Disorders as Discrete Clinical Conditions: Dimensional Versus Categorical Classification

THOMAS A. WIDIGER and WHITNEY L. GORE

"In *DSM-IV*, there [was] no assumption that each category of mental disorder is a completely discrete entity with absolute boundaries dividing it from other mental disorders or from no mental disorder" (American Psychiatric Association [APA], 2000, p. xxxi). This carefully worded disclaimer, however, was somewhat hollow, as it was the case that "*DSM-IV* [was] a categorical classification that divides mental disorders into types based on criterion sets with defining features" (APA, 2000, p. xxxi). The categorical model of classification is consistent with a medical tradition in which it is believed (and often confirmed in other areas of medicine) that disorders have specific etiologies, pathologies, and treatments (Guze, 1978; Guze & Helzer, 1987; Zachar & Kendler, 2007).

Clinicians, following this lead, diagnosed and conceptualized the conditions presented in *DSM-IV-TR* as disorders that are qualitatively distinct from normal functioning and from one another. *DSM-IV-TR* provided diagnostic criterion sets to help guide clinicians toward a purportedly correct diagnosis and an additional supplementary section devoted to differential diagnosis that indicated "how to differentiate [the] disorder from other disorders that have similar presenting characteristics" (APA, 2000, p. 10). The intention of the manual was to help the clinician determine which particular mental disorder provides the best explanation for the symptoms and problems facing the patient. Clinicians devote initial time with a new patient to identify, through differential diagnosis, which specific disorder best explains a patient's presenting complaints. The assumption is that the person is suffering from a single, distinct clinical condition, caused by a specific pathology for which there will be a specific treatment (Frances, First, & Pincus, 1995).

Authors of the diagnostic manual devote a considerable amount of time writing, revising, and researching diagnostic criteria to improve differential diagnosis. They buttress each disorder's criterion set, trying to shore up discriminant validity and distinctiveness, following the rubric of Robins and Guze (1970) that the validity of a diagnosis rests in large part on its "delimitation from other disorders" (p. 108). "These

criteria should . . . permit exclusion of borderline cases and doubtful cases (an undiagnosed group) so that the index group may be as homogeneous as possible" (Robins & Guze, 1970, p. 108).

Scientists may devote their careers to attempting to identify the specific etiology, pathology, or treatment for a respective diagnostic category. Under the assumption that the diagnoses do in fact refer to qualitatively distinct conditions, it follows that there should be a specific etiology, pathology, and perhaps even a specific treatment for each respective disorder. The theories, hypotheses, findings, and disputes regarding the specific etiology, pathology, and/or treatment of a respective mental disorder largely inform the respective chapters of professional, graduate, and undergraduate texts on psychopathology, such as this current edition of *Adult Psychopathology and Diagnosis*.

However, the question of whether mental disorders are, in fact, discrete clinical conditions or arbitrary distinctions along continuous dimensions of functioning has been a long-standing issue (Kendell, 1975) and its significance is escalating with the growing recognition of the limitations of the categorical model (Hyman, 2010; Widiger & Clark, 2000; Widiger & Samuel, 2005). The principal model for the validation of mental disorder diagnostic categories was provided by Robins and Guze (1970), who articulated five fundamental phases: clinical description, laboratory study, delimitation from other disorders, follow-up, and family studies. However, the research that has accumulated to date has not supported the validity of the delimitation of the disorders from one another. "Indeed, in the last 20 years, the categorical approach has been increasingly questioned as evidence has accumulated that the so-called categorical disorders like major depressive disorder and anxiety disorders, and schizophrenia and bipolar disorder seem to merge imperceptibly both into one another and into normality . . . with no demonstrable natural boundaries" (First, 2003, p. 661). As expressed by the vice chair of *DSM-5*, "the failure of DSM-III criteria to specifically define individuals with only one disorder served as an alert that the strict neo-Kraepelinian categorical approach to mental disorder diagnoses advocated by Robins and Guze (1970), Spitzer, Endicott, & Robins (1978), and others could have some serious problems" (Regier, 2008, p. xxi). As acknowledged by Kendell and Jablensky (2003), "it is likely that, sooner or later, our existing typology will be abandoned and replaced by a dimensional classification" (p. 8).

In 1999, a DSM-5 Research Planning Conference was held under joint sponsorship of the APA and the National Institute of Mental Health (NIMH), the purpose of which was to set research priorities that would optimally inform future classifications. One impetus for this effort was the frustration with the existing nomenclature.

In the more than 30 years since the introduction of the Feighner criteria by Robins and Guze, which eventually led to *DSM-III,* the goal of validating these syndromes and discovering common etiologies has remained elusive. Despite many proposed candidates, not one laboratory marker has been found to be specific in identifying any of the *DSM*-defined syndromes. Epidemiologic and clinical studies have shown extremely high rates of comorbidities among the disorders, undermining the hypothesis that the syndromes represent distinct etiologies. Furthermore, epidemiologic studies have shown a high degree of short-term diagnostic instability for many disorders. With regard to treatment, lack of treatment specificity is the rule rather than the exception (Kupfer, First, & Regier, 2002, p. xviii).

DSM-5 Research Planning Work Groups were formed to develop white papers that would set an effective research agenda for the next edition of the diagnostic manual. The Nomenclature Work Group, charged with addressing fundamental assumptions of the diagnostic system, concluded that it will be "important that consideration be given to advantages and disadvantages of basing part or all of DSM-V on dimensions rather than categories" (Rounsaville et al., 2002, p. 12).

The white papers developed by the DSM-5 Research Planning Work Groups were followed by a series of international conferences whose purpose was to further enrich the empirical data base in preparation for the eventual development of *DSM-5* (a description of this conference series can be found at www.dsm5.org). The first conference was devoted to shifting personality disorders to a dimensional model of classification (Widiger, Simonsen, Krueger, Livesley, & Verheul, 2005). The final conference was devoted to dimensional approaches across the diagnostic manual, including substance use disorders, major depressive disorder, psychoses, anxiety disorders, and developmental psychopathology, as well as the personality disorders (Helzer, Kraemer, et al., 2008).

In the introduction to *DSM-5* (APA, 2013), the apparent failure of the categorical model of classification is duly noted. "The historical aspiration of achieving diagnostic homogeneity by progressively subtyping within disorder categories no longer is sensible; like most common human ills, mental disorders are heterogeneous at many levels, ranging from genetic risk factors to symptoms" (APA, 2013, p. 12). It was a major purpose of the authors of *DSM-5* to have this new edition of the diagnostic manual be "central to the development of dimensional approaches to diagnosis that will likely supplement or supersede current categorical approaches in the coming years" (APA, 2013, 13). However, as will be discussed herein, the diagnoses of *DSM-5* remain largely categorical.

The purpose of this chapter is to review the *DSM-IV-TR* and *DSM-5* categorical diagnostic approach. The chapter begins with a discussion of the problematic boundaries among the *DSM-IV-TR* and *DSM-5* categorical diagnoses. We then focus in particular on depression, alcohol abuse and dependence, personality disorders, and intellectual disability. We conclude with a discussion of the shifts within *DSM-5* toward a dimensional classification.

DIAGNOSTIC BOUNDARIES

In an effort to force differential diagnosis, a majority of diagnoses in *DSM-III* (APA, 1980) contained exclusionary criteria specifying that a respective disorder could not be diagnosed if it occurred in the presence of another disorder. These exclusions by fiat did not prove to be effective (Boyd et al., 1984) and many were deleted in *DSM-III-R* (APA, 1987). As expressed at the time by Maser and Cloninger (1990), "it is clear that the classic Kraepelinian model in which all psychopathology is comprised of discrete and mutually exclusive diseases must be modified or rejected" (p. 12).

Many *DSM-5* diagnostic criterion sets, however, continue to include exclusionary criteria that attempt to force clinicians to make largely arbitrary choices among alternative diagnoses (APA, 2013), and it is also evident that there will likely continue to be a highly problematic rate of diagnostic co-occurrence (Kessler, Chiu, Demler, & Walters, 2005; Krueger & Markon, 2006; Maser & Patterson, 2002; Widiger & Clark,

2000). The term *comorbidity* refers to the co-occurrence of distinct disorders, apparently interacting with one another, each presumably with its own etiology, pathology, and treatment implications (Feinstein, 1970). If one considers the entire diagnostic manual (which has not yet been done by any epidemiological study), it would likely be exceedingly rare for any patient to meet the criteria for just one disorder, and the comorbidity rises even further if one considers lifetime co-occurrence. Brown, Campbell, Lehman, Grisham, and Mancill (2001) reported that 95% of individuals in a clinical setting who meet criteria for lifetime major depression or dysthymia also meet criteria for a current or past anxiety disorder. In the case of psychopathology, comorbidity may be saying more about the invalidity of existing diagnostic distinctions than the presence of multiple coexisting conditions (Krueger, 2002; Widiger & Edmundson, 2011).

Diagnostic comorbidity has become so prevalent that some researchers have argued for an abandonment of the term *comorbidity* in favor of a term (e.g., *co-occurrence*) that is more simply descriptive and does not imply the presence of distinct clinical entities (Lilienfeld, Waldman, & Israel, 1994). There are instances in which the presence of multiple diagnoses suggests the presence of distinct yet comorbid psychopathologies, but in most instances the presence of co-occurring diagnoses does appear to suggest the presence of a common, shared pathology and, therefore, a possible failing of the current diagnostic system (Krueger & Markon, 2006; Widiger & Clark, 2000). "Comorbidity may be trying to show us that many current treatments are not so much treatments for transient 'state' mental disorders of affect and anxiety as they are treatments for core processes, such as negative affectivity, that span normal and abnormal variation as well as undergird multiple mental disorders" (Krueger, 2002, p. 44).

Diagnostic criteria have traditionally been developed and modified in order to construct a disorder that is as homogeneous as possible, thereby facilitating the likelihood of identifying a specific etiology, pathology, and treatment (Robins & Guze, 1970). However, the typical result of this effort is to leave many cases unaccounted for. In addition, despite the best effort to construct homogeneous and distinct syndromes, *DSM-IV-TR* was still replete with heterogeneous conditions with overlapping boundaries (Smith & Combs, 2010). New diagnostic categories are added to the nomenclature in large part to decrease clinicians' reliance on the nonspecific, wastebasket label of "not otherwise specified" (NOS). NOS was among the most frequent disorders within clinical populations (Widiger & Edmundson, 2011). The function of many of the new disorders that have been added to recent editions of the manual have not involved the identification of uniquely new forms of psychopathology. Their purpose was generally instead to fill problematic gaps. Notable examples for *DSM-IV* included bipolar II (filling a gap between *DSM-III-R* bipolar and cyclothymic mood disorders), mixed anxiety-depressive disorder (a gap between anxiety and mood disorders), depressive personality disorder (personality and mood disorders), postpsychotic depressive disorder of schizophrenia (schizophrenia and major depression) (Frances et al., 1995).

When new diagnoses are added to fill gaps, they have the ironic effect of creating additional boundary problems, thereby making differential diagnosis even more problematic (Phillips, Price, Greenburg, & Rasmussen, 2003; Pincus, Frances, Davis, First, & Widiger, 1992; Pincus, McQueen, & Elinson, 2003). One must ask, for instance,

whether it is really meaningful or useful to determine whether mixed anxiety-depressive disorder is a mood or an anxiety disorder, whether schizoaffective disorder is a mood disorder or a form of schizophrenia (Craddock & Owen, 2010, whether postpsychotic depressive disorder of schizophrenia is a form of depression or schizophrenia, whether early onset dysthymia is a mood or a personality disorder (Widiger, 2003), whether acute stress disorder is an anxiety or a dissociative disorder (Cardena, Butler, & Spiegel, 2003), whether hypochondriasis is an anxiety disorder or a somatoform disorder, whether body dysmorphic disorder is an anxiety, eating, or somatoform disorder, and whether generalized social phobia is an anxiety or a personality disorder (Widiger, 2001a). In all these cases the most accurate answer is likely to be that each respective disorder includes features of different sections of the diagnostic manual. Yet the arbitrary and procrustean decision of which single section of the manual in which to place each diagnosis must be made by the authors of a categorical diagnostic manual, and a considerable amount of effort and research is conducted to guide this decision, followed by further discussion and research to refute and debate whatever particular categorical decision was made.

There are comparable examples of what might be arbitrary splitting of categories in *DSM-5* (APA, 2013). *DSM-5* split out from reactive attachment disorder a new diagnosis of disinhibited social engagement disorders. Binge eating disorder (which was originally included within the diagnosis of bulimia nervosa) obtained official recognition. However, for the most part, changes that occurred in *DSM-5* were consistent with the intention to shift the manual more closely to a dimensional model. For example, there are cases in which previously "distinct" diagnoses were lumped together rather than split apart. For example, *DSM-5* autism spectrum disorder subsumes within one diagnosis *DSM-IV-TR* autistic disorder, Asperger's disorder, childhood disintegrative disorder, and pervasive developmental disorder not otherwise specified. The archaic subtypes of schizophrenia were deleted. "Instead a dimensional approach to rating severity of core symptoms of schizophrenia is included in *DSM-5* Section III" (APA, 2013, p. 810). The *DSM-IV-TR* diagnoses of somatization disorder, hypochondriasis, and pain disorder were all subsumed within one diagnosis of somatic symptom disorder. Pathological gambling was lumped with substance use disorders within a new section concerning addictive disorders, and substance abuse and dependence are no longer conceptualized as categorically distinct conditions. Included in Section III of *DSM-5* is a proposed dimensional trait model that would subsume all of the existing personality disorder categories.

Depression

Mood disorders is a section of the APA diagnostic manual for which the presence of qualitatively distinct conditions is particularly difficult to defend, especially for the primary diagnoses of dysthymia and major depressive disorder. Discussed here will be early onset dysthymia, the continuum of depression, and subthreshold major depression, along with more general points concerning the boundary between mood and personality disorder.

There is no meaningful distinction between early-onset dysthymia, an officially recognized mood disorder diagnosis, and depressive personality disorder, a diagnosis

proposed for *DSM-IV* but included within its appendix (APA, 2000). In fact, much of the empirical and conceptual basis for adding dysthymia to the *DSM-III* (APA, 1980) came from research and clinical literature concerning depressive personality (i.e., Keller, 1989). As acknowledged by the principal architects of *DSM-III,* dysthymia is "roughly equivalent to the concept of depressive personality" (Spitzer, Williams, & Skodol, 1980, p. 159). Depressive personality disorder was included within the mood disorders section of *DSM-III* despite the recommendations to recognize its existence as a disorder of personality (Klerman, Endicott, Spitzer, & Hirschfeld, 1979) because it resembled the symptomatology of other mood disorders (i.e., depressed mood) more than it resembled the symptoms of other personality disorders (e.g., schizoid). However, whereas mood disorders are defined largely by similarity in content (i.e., mood being the predominant feature; APA, 2013), the personality disorders are defined largely by form (i.e., early onset, pervasive, and chronic) often with quite different content (e.g., schizoid also shares little resemblance to histrionic personality disorder).

After *DSM-III* was published, it became evident that many of the persons who were consistently and characteristically pessimistic, gloomy, cheerless, glum, and sullen (i.e., dysthymic) had been that way since childhood and that in many cases no apparent or distinct age of onset could be established. In other words, its conceptualization as a personality disorder became apparent. *DSM-III-R,* therefore, added an early-onset subtype (APA, 1987) and acknowledged that "this disorder usually begins in childhood, adolescence, or early adult life, and for this reason has often been referred to as a Depressive Personality" (APA, 1987, p. 231).

Personality disorder researchers proposed again for *DSM-IV* to include a depressive personality disorder diagnosis. They were told that in order for it to be included, it needed to be distinguished from the already established diagnosis of early-onset dysthymia, a task that might be considered rather difficult, if not unfair, given that the latter construct was based in large part on the former construct. Nevertheless, the DSM-IV Personality Disorders Work Group developed a proposed diagnostic criterion set that placed relatively more emphasis on cognitive features not currently included within the criterion set for dysthymia (including early-onset), as well as excluding somatic features (Task Force on DSM-IV, 1991). This criterion set was provided to the DSM-IV Mood Disorders Work Group to include within their *DSM-IV* field trial to determine empirically whether it was indeed possible to demarcate an area of functioning not yet covered by early-onset dysthymia, or at least identify persons not yet meeting diagnostic criteria for early-onset dysthymia.

The proposed criterion set was successful in reaching this goal (Phillips et al., 1998), which, perhaps, should not be surprising because no criterion set for a categorical diagnosis appears to be entirely successful in covering all cases. However, the Mood Disorders Work Group was equally impressed with the potential utility of the depressive personality diagnostic criteria for further describing and expanding the coverage of dysthymia (Keller et al., 1995) and, therefore, incorporated much of the proposed criteria for depressive personality into their proposed revisions for dysthymia, including early-onset (Task Force on DSM-IV, 1993). The DSM-IV Task Force recognized that it might be problematic to now require the personality disorder researchers to further redefine depressive personality to

distinguish it from this further revision of dysthymia. Therefore, the DSM-IV Task Force decided instead to include both criterion sets in the appendix to *DSM-IV* (along with the original criterion set for dysthymia within the mood disorders section), with the acknowledgment that there may not be any meaningful distinction between them (APA, 1994; Frances et al., 1995). However, depressive personality disorder was not even included within the appendix for *DSM-5.* Dysthymia and chronic major depressive disorder are now collapsed within persistent depressive disorder in *DSM-5.*

The Continuum of Depression The common view is that many instances of sadness (or even depression) do not constitute a mental disorder. Persons can be very sad without having a mental disorder (Horwitz & Wakefield, 2007). However, a simple inspection of the diagnostic criteria for major depressive disorder would not lend confidence to a conceptualization of this condition as being qualitatively distinct from "normal" depression or sadness (Andrews et al., 2008). Persons who are just very sad will have most of the same attributes (if not all of them) but just at a lesser degree of severity. The diagnostic criteria for major depressive disorder include depressed mood, loss of interest or pleasure, weight loss (or gain), insomnia (or hypersomnia), psychomotor retardation (or agitation), loss of energy, feelings of worthlessness, and/or diminished capacity to make decisions (APA, 2013). Each of these diagnostic criteria is readily placed along a continuum of severity that would shade imperceptibly into what would be considered a "normal" sadness or depression. *DSM-5,* therefore, includes specific thresholds for each of them, but they are clearly arbitrary thresholds that simply demarcate a relatively higher level of severity from a lower level of severity (e.g., "nearly every day" or "markedly diminished," and at least a "2-week" period; APA, 2013, p. 188). The diagnosis requires five of these nine criteria, with no apparent rationale for this threshold other than it would appear to be severe enough to be defensible to be titled as a "major" depressive episode, as distinguished from a "minor" depressive episode, which is then distinguished from "normal" sadness (APA, 2013).

Depression does appear to shade imperceptibly into "normal" sadness (Andrews et al., 2008). Üstün and Sartorius (1995) conducted a study of 5,000 primary-care patients in 14 countries and reported a linear relationship between disability and number of depressive symptoms. Kessler, Zhao, Blazer, and Swartz (1997) examined the distribution of minor and major symptoms of depression using data from the National Comorbidity Survey. They considered the relationship of these symptoms with parental history of mental disorder, number and duration of depressive episodes, and comorbidity with other forms of psychopathology. Respective relationships increased with increasing number of symptoms, with no clear, distinct break. Sakashita, Slade, and Andrews (2007) examined the relationship between the number of symptoms of depression and four measures of impairment using data from the Australian National Survey of Mental Health and Well-Being, and found that the relationship was again simply linear, with no clear or natural discontinuity to support the selection of any particular cutoff point.

Taxometrics refers to a series of related statistical techniques to detect whether a set of items is optimally understood as describing (assessing) a dimensional or a categorical construct (Beauchaine, 2007; Ruscio & Ruscio, 2004). Other statistical

techniques, such as cluster or factor analyses, presume that the construct is either categorical or dimensional (respectively) and then determines how best to characterize the variables or items in either a categorical or dimensional format (respectively). Taxometric analyses are uniquely intriguing in providing a direct test of which structural model is most valid in characterizing the set of items or variables.

A number of taxometric studies have been conducted on various symptoms and measures of depression. The first was provided by Ruscio and Ruscio (2000) in their taxometric analyses of items from the Beck Depression Inventory and, independently, items from the Zung Self-Rating Depression Scale in a sample of 996 male veterans who had received a diagnosis of post-traumatic stress disorder but also had a high prevalence rate of major depressive disorder, as well as a sample of 8,045 individuals from the general population (60% female) who completed the items from the Depression scale of the Minnesota Multiphasic Personality Inventory. They indicated that "results of both studies, drawing on three widely used measures of depression, corroborated the dimensionality of depression" (Ruscio & Ruscio, 2000, p. 473).

The taxometric findings of Ruscio and Ruscio (2000) have been subsequently replicated, including taxometric analyses of (a) structured interview assessments of *DSM-IV-TR* major depressive disorder symptoms and, independently, items from the Beck Depression Inventory in a sample of 960 psychiatric outpatients (Slade, 2007), (b) major depressive disorder diagnostic criteria assessed in the 1,933 persons who endorsed at least one criterion in the Australian National Survey of Mental Health and Well-Being (Slade & Andrews, 2005), (c) self- and parent-reported depressive symptoms in 845 children and adolescents drawn from the population-based Georgia Health and Behavior Study (Hankin, Fraley, Lahey, & Waldman, 2005), (d) responses to MMPI-2 depression scales completed by 2,000 psychiatric inpatients and outpatients (Franklin, Strong, & Greene, 2002), (e) epidemiologic survey of depressive symptoms within 392 college students (Baldwin & Shean, 2006), (f) Beck Depression Inventory items reported by 2,260 college students (Ruscio & Ruscio, 2002), and (g) depression items in the Composite International Diagnostic Interview as administered in the National Comorbidity Survey to 4,577 participants who endorsed the item concerning a lifetime occurrence of sad mood or loss of interest (Prisciandoro & Roberts, 2005). However, in contrast to the findings from these eight taxometric studies, three taxometric studies have supported a latent class taxon, including semistructured interview assessments of *DSM-IV-TR* major depressive disorder symptoms in 1,800 psychiatric outpatients (Ruscio, Zimmerman, McGlinchey, Chelminski, & Young, 2007), interview and self-report assessments of depression in 1,400 high school students (Solomon, Ruscio, Seeley, & Lewinsohn, 2006), and self-report and interview data on depression in 378 adolescents receiving treatment for depression (Ambrosini, Bennett, Cleland, & Haslam, 2002). In sum, the bulk of the evidence does appear to support a dimensional understanding of depression, but there is some ambiguity and inconsistency in the taxometric findings (Beach & Amir, 2003; Beauchaine, 2007; Widiger, 2001b).

Subthreshold Major Depression Depression is a section of the diagnostic manual that does have considerable difficulty identifying or defining a clear boundary with "normal" sadness. Subthreshold cases of depression (i.e., persons with depressive

symptoms below the threshold for a *DSM-5* mental disorder diagnosis) are clearly responsive to pharmacologic interventions, do seek treatment for their sadness, and are often being treated within primary care settings (Judd, Schettler, & Akiskal, 2002; Pincus et al., 2003). These facts contributed to the proposal to include within an appendix to *DSM-IV* a diagnosis of "minor depressive disorder," which it is acknowledged "can be difficult to distinguish from periods of sadness that are an inherent part of everyday life" (APA, 2000, p. 776).

Wakefield (2007) has been critical of the criteria for major depressive disorder for including an inconsistently applied exclusion criterion. The *DSM-IV-TR* excluded most instances of depressive reactions to the loss of a loved one (i.e., uncomplicated bereavement). Depression after the loss of a loved one could be considered a mental disorder if "the symptoms persist for longer than 2 months" (APA, 2000, p. 356). Allowing persons just 2 months to grieve before one is diagnosed with a mental disorder does appear to be rather arbitrary. More importantly, it is also unclear if depression in response to other losses should not also then be comparably excluded, such as depression secondary to the loss of a job or physical health (Wakefield, Schimtz, First, & Horwitz, 2007). Why the loss of a person is treated so differently from the loss of health or a job is not clear.

On the other hand, one could argue alternatively that all exclusion criteria should be removed. Perhaps the problem is not that depression in response to a loss of a job or physical disorder should not be a disorder, analogous to bereavement (Wakefield, 2007); perhaps the problem is that bereavement should be a mental disorder (Bonanno et al., 2007; Forstmeier & Maercker, 2007; Widiger & Miller, 2008). What is currently considered to be a normal depression in response to the loss of a loved one does often, if not always, include pain and suffering, meaningful impairment to functioning, and is outside of the ability of the bereaved person to fully control, the essential hallmarks of a mental disorder (Widiger & Sankis, 2000). The depression is a reasonable response to the loss of a loved one, a psychological trauma, but many physical disorders and injuries are reasonable and understandable responses to a physical trauma. The loss is perhaps best understood as part of the etiology for the disorder, not a reason for which a disorder is not considered to be present (Widiger, 2012a).

One of the major revisions for *DSM-5* was indeed to weaken the distinction between normal bereavement and a mental disorder of depression. *DSM-5* no longer excludes the diagnosis of a major depressive disorder if the depression is secondary to the loss of a loved one. "Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability)" (APA, 2013, p. 161) can now all be diagnosed as a mental disorder.

Alcohol Abuse and Dependence

One of the sections of the diagnostic manual for which a categorical model of classification and conceptualization has had a firmly entrenched tradition has been the substance use disorders. Alcoholism in particular has long been conceptualized as a qualitatively distinct disease (Garbutt, 2008; Goodwin & Guze, 1996). A significant change to its diagnosis and conceptualization occurred with *DSM-III-R* (APA, 1987) when it shifted from being understood as a purely physiological dependence to a broader and less specific behavioral dependence (Carroll,

Rounsaville, & Bryant, 1994; Edwards & Gross, 1976). "Dependence is seen as a complex process that reflects the central importance of substances in an individual's life, along with a feeling of compulsion to continue taking the substance and subsequent problems controlling use" (Schuckit et al., 1999, p. 41). To many, though, the diagnosis does still refer to a disease, but one that is developed through a normal social-learning history (Kandel, 1998).

However, the diagnosis has been broadened considerably in *DSM-5* wherein it is referred to as a behavioral addiction, and would, therefore, be listed along with pathological gambling (Martin, 2005; Petry, 2006; Potenza, 2006). Pathological gambling has been considered by many substance use and pathological gambling researchers and clinicians to be an addiction, but it could not be included within the substance related disorders section because it does not involve the ingestion of a substance (Bradford, Geller, Lesieur, Rosenthal, & Wise, 1996). This requirement has been deleted in *DSM-5,* with the section renamed "substance-related and addictive disorders" (APA, 2013).

This new class of disorders could eventually contain a wide variety of possible behavioral addictions, including an excessive participation in shopping, sex, or the Internet. As stated at one point on the *DSM-5* website, along with pathological gambling, "other addiction-like behavioral disorders such as 'Internet addiction' . . . will be considered as potential additions to this category as research data accumulate" (APA, 2010, "Substance Related Disorders," para. 1). The preface to this section of the diagnostic manual explicitly states that Internet, sex, and shopping addictions are not included because there is currently insufficient evidence to support their validity. However, it is apparent that the broadening of the concept of substance dependence to include behavioral forms of addiction will encourage clinicians to diagnose these additional variants. "This 'slippery slope' makes it difficult to know where to draw the line demarcating any excessive behavior as an addiction" (Petry, 2005a, p. 7). Provided within an appendix to *DSM-5* for conditions needing further study is Internet gaming disorder (i.e., behavioral addiction on Internet games), including its diagnostic criteria, risk factors, prevalence, and differential diagnosis. Proposed for inclusion in the sex disorders section of *DSM-5* was hypersexual disorder, which can indeed be identified as a sex addiction (Kafka, 2010; Ragan & Martin, 2000; Winters, 2010).

The distinction between harmful substance use and a substance use disorder is itself unclear and indistinct. Presumably, persons can choose to consume alcohol without being compelled to do so by the presence of a mental disorder. The *DSM-5* diagnostic criteria for a substance use disorder are fallible indicators for harmful and dyscontrolled usage (e.g., use more than originally intended, continue to use despite social consequences, and reduction of other activities in preference for the substance; APA, 2013). The more of these indicators of dyscontrol that are present, the more likely that there is in fact dyscontrol, but none can be considered infallible in the identification of dyscontrol and no particular number of them clearly demarcates a boundary between the presence versus absence of dyscontrolled usage. It is not even clear how much purportedly volitional or regulatory control a normal, healthy person has over adaptive, healthy behaviors (Bargh & Ferguson, 2000; Howard & Conway, 1986; Kirsch & Lynn, 2000; Wegner & Wheatley, 2000), let alone the boundary between controlled and dyscontrolled harmful behaviors. Both normal and abnormal human functioning is, at best, the result of a complex

interaction of apparent volitional choice with an array of biogenetic and environmental determinants.

The distinction between *DSM-IV-TR* alcohol abuse and dependence was equally fuzzy. Abuse has generally been considered to be simply a residual category and/or a less severe form of dependence (Saunders, 2006). Some of the diagnostic criteria for abuse were contained with the criterion set for dependence (e.g., interference with social, occupational, or recreational activities), which is always a problem for disorders that would be considered to be qualitatively distinct. It is largely for this reason that the formal distinction between abuse and dependence was abandoned in *DSM-5* (APA, 2013).

The diagnostic criteria for alcohol dependence were written largely in an effort to describe a prototypic case of the disorder, a practice that is still followed for all but a few of the disorders throughout *DSM-5*. However, prototypic cases are typically understood to be the most severe cases and/or the cases that involve all possible features or symptoms of the disorder (First & Westen, 2007). The construction of diagnostic criterion sets in terms of prototypic cases does work to an extent, but it also fails to adequately describe many of the actual cases, including the subthreshold cases, and perhaps even the typical cases, depending upon the distribution of features and symptomatology within the population. Constructing criterion sets in terms of prototypic cases can be comparable to confining the description and diagnosis of (for instance) intellectual disability to the most severe variant, and then attempting to apply this description to mild and moderate variants; a method of diagnosis that would obviously be sorely limited. The limitations of this approach are now becoming more closely appreciated in the diagnosis of dyscontrolled substance use and, more specifically, alcohol use disorders, where the existing criterion sets are failing to adequately describe (for instance) dyscontrolled and impairing alcohol usage in adolescents (Crowley, 2006) and other "diagnostic orphans" (Saunders, 2006).

The limitation is perhaps most clearly demonstrated in studies using item response theory (IRT) methodology. IRT allows the researcher to investigate the fidelity with which items are measuring a latent trait along the length of its continuum, contrasting, for instance, the amount of information that different diagnostic criteria provide at different levels of the latent trait (Muthen, 2006). Some diagnostic criteria, for instance, might be most useful in distinguishing among mild cases of the disorder, whereas other diagnostic criteria are most useful in distinguishing among the more severe cases of the disorder. A number of IRT analyses have now been conducted for the diagnosis of substance dependence (and other disorders) and the findings are remarkably consistent (Reise & Waller, 2009). The existing diagnostic criterion sets (and/or symptoms currently assessed in existing instruments) cluster around the high end of the disorder as opposed to being spread out across the entire range of the continuum (e.g., Kahler & Strong, 2006; Langenbucher et al., 2004; Muthen, 2006; Proudfoot, Baillie, & Teesson, 2006; Saha, Chou, & Grant, 2006). This consistent pattern of results is in stark contrast to what is traditionally found in cognitive ability testing, where IRT analyses have been largely developed and previously applied (Reise & Waller, 2009).

It is evident from the IRT analyses that the existing diagnostic criterion sets are sorely inadequate in characterizing the lower and even middle range of substance use

dysfunction, consistent with the *DSM-IV-TR* and *DSM-5* descriptions being confined to a prototypic case (of the presumably qualitatively distinct disorder). If alcohol usage was conceptualized along a continuum, the job of the authors of the diagnostic manual would be to construct a description and measurement of the disorder that adequately represents each of the levels or degrees to which the disorder appears along this continuum rather than attempt to describe the prototypic case. The *DSM-IV-TR* criterion set was confined to the most severe cases and was not describing well a large proportion of persons with clinically significant alcohol use dysfunction. As a result, clinicians had to rely on the nondescriptive, wastebasket diagnosis of NOS to describe the lower range of the continuum (Saunders, 2006).

A step in the direction of recognizing the continuous nature of substance use disorder was incorporated in *DSM-5.* Along with the abandonment of the distinction between abuse and dependence, *DSM-5* also includes a rating of severity for a substance use disorder, depending upon the number of diagnostic criteria that are met. For example, a "mild" substance use disorder is suggested by the presence of just two to three features (APA, 2013). However, the features for the mildest and the most severe cases are still the same. What would be more informative would be to have the different levels be defined by the features that are relatively specific to that level, analogous to how the comparable distinctions are made between the levels of severity for an intellectual disability.

Personality Disorders

There are three major problematic boundaries for the personality disorders: the boundaries between personality disorders and other mental disorders, the boundaries between personality disorders and normal personality, and the boundaries among the personality disorders. Discussed first will be the boundaries with other mental disorders, followed by the other two boundaries.

Boundaries With Other Mental Disorders Among the proposals considered for the personality disorders at the DSM-5 Research Planning Conference (Kupfer et al., 2002) was the suggestion to replace the diagnosis of personality disorder with early onset and chronic variants of existing Axis I mental disorders (First et al., 2002). This might appear at first blush to be a radical proposal, and perhaps it is. However, it does have support from a variety of sources.

There is no clear or consistent boundary between the personality disorders and many other mental disorders, particularly the mood, anxiety, impulse dyscontrol, and psychotic disorders (Krueger, 2005). In fact, *DSM-5* schizotypal personality disorder has long been classified as a form of schizophrenia rather than as a personality disorder in the World Health Organization's *International Classification of Diseases* (*ICD-10*; WHO, 1992), the parent classification for the APA's *DSM-5*. Schizotypal personality disorder is genetically related to schizophrenia, most of its neurobiological risk factors and psychophysiological correlates are shared with schizophrenia (e.g., eye tracking, orienting, startle blink, and neurodevelopmental abnormalities), and the treatments that are effective in ameliorating schizotypal symptoms overlap with treatments used for persons with Axis I schizophrenia (Kwapil & Barrantes-Vidal, 2012).

On the other hand, there are also compelling reasons for continuing to consider schizotypal as a personality disorder (Kwapil & Barrantes-Vidal, 2012; Raine, 2006). Simply because a personality disorder shares a genetic foundation with another disorder does not then indicate that it is a form of that other disorder. Contrary to viewing schizotypal personality disorder as a variant of schizophrenia is that the disorder is far more comorbid with other personality disorders than it is with any other schizophrenia-related disorder, persons with schizotypal personality disorder rarely go on to develop schizophrenia, and schizotypal symptomatology is seen in quite a number of persons within the general population who lack any genetic association with schizophrenia and who would not be appropriately described as having some form of schizophrenia (Raine, 2006).

However, a fate similar to that of schizotypal personality disorder in *ICD-10* (WHO, 1992) and depressive personality disorder in *DSM-IV* (APA, 1994) could await the other personality disorder diagnostic categories in a future edition of the diagnostic manual (First et al., 2002). For example, social phobia was a new addition to *DSM-III* (Spitzer et al., 1980; Turner & Beidel, 1989). It was considered then to be a distinct, circumscribed condition, consistent with the definition of a phobia as a "persistent, irrational fear of a *specific* object, activity, or situation" (APA, 1994, p. 336, our emphasis). However, it became apparent to anxiety disorder researchers and clinicians that the fears of many of their patients were rarely so discrete and circumscribed (Spitzer & Williams, 1985). Therefore, the authors of *DSM-III-R* developed a generalized subtype for when "the phobic situation includes most social situations" (APA, 1987, p. 243). *DSM-III-R* generalized social phobia, however, merged into the *DSM-III* diagnosis of avoidant personality disorder. Both were concerned with a pervasive, generalized social insecurity, discomfort, and timidity. Efforts to distinguish them have indicated only that avoidant personality disorder tends to be, on average, relatively more dysfunctional than generalized social phobia (Sanislow, da Cruz, Gianoli, & Reagan, 2012; Turner, Beidel, & Townsley, 1992).

DSM-IV provided no solution. In fact, it was acknowledged that generalized social phobia emerged "out of a childhood history of social inhibition or shyness" (APA, 1994, p. 414), consistent with the concept of a maladaptive personality trait. An argument raised for classifying this condition as an anxiety disorder rather than as a personality disorder was that many persons with the disorder benefit from pharmacologic interventions (Liebowitz, 1992). "One may have to rethink what the personality disorder concept means in an instance where 6 weeks of phenelzine therapy begins to reverse long-standing interpersonal hypersensitivity as well as discomfort in socializing" (Liebowitz, 1992, p. 251). Of course, one might also have to rethink what the anxiety disorder concept means when an antidepressant is an effective form of treating an anxiety disorder. In addition, it is unclear why a maladaptive personality trait should not be responsive to a pharmacologic intervention (Knorr & Kessing, 2010; Knutson et al., 1998; Tang et al., 2009). In any case, the authors of *DSM-IV-TR* concluded that these two conditions "may be alternative conceptualizations of the same or similar conditions" (APA, 2000, p. 720).

There does not currently appear to be a meaningful distinction between avoidant personality disorder and generalized social phobia (APA, 2000; Sanislow et al., 2012; Tyrer, 2005; Widiger, 2003). Some suggest that the best solution is to simply abandon the personality disorder diagnosis in favor of the generalized anxiety disorder (First

et al., 2002; Schneider, Blanco, Anita, & Liebowitz, 2002). "We believe that the more extensive evidence for syndromal validity of social phobia, including pharmacological and cognitive-behavioral treatment efficacy, make it the more useful designation in cases of overlap with avoidant personality" (Liebowitz et al., 1998, p. 1060). The reference to treatment efficacy by Liebowitz et al. (1998) falls on receptive ears for many clinicians who struggle to obtain insurance coverage for the treatment of maladaptive personality functioning. It is often reported that a personality disorder diagnosis is stigmatizing, due in large part to its placement on a distinct axis that carries the implication of being an untreatable, lifetime disorder (Frances et al., 1991; Kendell, 1983). For reasons such as these, the Assembly of the American Psychiatric Association (which has authoritative governance over the approval of revisions to the diagnostic manual) has repeatedly passed resolutions to explore proposals to move one or more personality disorders to Axis I in large part to address the stigma and lack of reimbursement for their treatment. This proposal is now moot, given the abandonment of the multiaxial system in *DSM-5* (APA, 2013). Future proposals of the Assembly though might now take the form of shifting individual personality disorders into a respective mood, anxiety, or impulse dyscontrol disorder as an early onset, chronic variant.

Just as the depressive, schizotypal, and avoidant personality disorders could be readily subsumed within an existing section of Axis I, borderline personality disorder could be reclassified as a mood dysregulation and/or impulse dyscontrol disorder; obsessive-compulsive personality disorder could be reclassified as a generalized and chronic variant of obsessive-compulsive anxiety disorder (although there is in fact only weak evidence to support a close relationship between the obsessive-compulsive anxiety and personality disorders; Samuels & Costa, 2012); and antisocial personality disorder by an adult variant of conduct (disruptive behavior) disorder. In *DSM-5,* schizotypal personality disorder is cross-listed within the schizophrenia spectrum section, and antisocial is cross-listed within the disruptive behavior disorders section (APA, 2013).

In sum, the future for many of the personality disorder diagnostic categories might be reformulations as early-onset chronic variants of existing Axis I disorders, as explicitly proposed at the initial DSM-5 Research Planning Conference (First et al., 2002). A difficulty with respect to this proposal, beyond the fundamental concern that the diagnostic manual would no longer recognize the existence of maladaptive personality functioning, is that it might just create more problems than it solves (Widiger, 2003). It is well established that persons have constellations of maladaptive personality traits that have significant consequential life outcomes (Ozer & Benet-Martinez, 2006; Roberts & DelVecchio, 2000). These personality traits are not currently well described by just one or even multiple personality disorder diagnoses (Clark, 2007; Trull & Durrett, 2005; Widiger, 2012b) and will be described even less well by multiple diagnoses across the broad classes of mood, anxiety, impulse dyscontrol, psychotic, and disruptive behavior disorders.

Boundaries With Other Personality Disorders and Normal Personality Rounsaville et al. (2002) suggested that the first section of the diagnostic manual to shift to a dimensional classification should be the personality disorders. The personality disorders have been among the most problematic of disorders to be diagnosed categorically (First et al.,

2002; Kendell, 1989). It is the norm for patients to meet diagnostic criteria for more than one personality disorder (Clark, 2007; Lilienfeld et al., 1994; Livesley, 2003; Trull & Durrett, 2005). Excessive diagnostic co-occurrence was in fact the primary reason that 5 of the 10 personality disorder diagnoses were proposed for deletion in *DSM-5* (Skodol, 2012). The excessive co-occurrence may be the result of the nature of the construct of personality. For instance, it is perhaps self-evident that persons are not well described by just one trait term (e.g., introverted). Each person has instead a constellation of personality traits, many of which are adaptive, and some of which may also be maladaptive. There is little reason to think that it would be different when a person is said to have a personality disorder (Widiger & Trull, 2007).

There also appears to be no clear or distinct boundary between normal and abnormal personality functioning. The *DSM-IV-TR* diagnostic thresholds were not set at a point that has any theoretical or clinical significance. They were arbitrarily set at half or one more than half of the diagnostic criteria (APA, 2000). In fact, all the personality disorders are readily understood as extreme and/or maladaptive variants of normal personality traits distributed within the general population; more specifically, the domains and facets of the five-factor dimensional model (FFM) of general personality structure (Widiger, Samuel, Mullins-Sweatt, Gore, & Crego, 2012; Widiger & Trull, 2007).

The FFM consists of five broad domains of general personality functioning: neuroticism (or emotional instability), extraversion versus introversion, openness versus closedness, agreeableness versus antagonism, and conscientiousness versus undependability. The FFM was derived originally through empirical studies of the trait terms within the English language (L. Goldberg, 1993). Language can be understood as a sedimentary deposit of the observations of persons over the thousands of years of the language's development and transformation. The most important domains of personality functioning are those with the most number of trait terms to describe and differentiate the various manifestations and nuances of a respective domain, and the structure of personality is suggested by the empirical relationships among these trait terms. The initial lexical studies with the English language converged well onto a five-factor structure (L. Goldberg, 1993). Subsequent lexical studies have been conducted on many additional languages (e.g., German, Dutch, Czech, Polish, Russian, Italian, Spanish, Hebrew, Hungarian, Turkish, Korean, & Filipino) and these have confirmed well the existence of the five broad domains (Church, 2001). The five broad domains have been differentiated into more specific facets by Costa and McCrae (1992) on the basis of their development of and research with the NEO Personality Inventory-Revised (NEO PI-R), by far the most commonly used and heavily researched measure of the FFM.

Studies have now well documented that all of the *DSM-IV-TR* personality disorder symptomatology is readily understood as maladaptive variants of the domains and facets of the FFM (O'Connor, 2002, 2005; Samuel & Widiger, 2008; Saulsman & Page, 2004; Widiger & Costa, 2002; Widiger et al., 2012). Saulsman and Page (2004) concluded, "each of the personality disorders shows associations with the five-factor model that are meaningful and predictable given their diagnostic criteria" (p. 1075). As acknowledged by Livesley (2001b), "all categorical diagnoses of *DSM* can be accommodated within the five-factor framework" (p. 24). As expressed by Clark (2007), "the five-factor model of personality is widely accepted as representing the higher-order

structure of both normal and abnormal personality traits" (p. 246). The problematic diagnostic co-occurrence among the *DSM-IV-TR* personality disorders is well explained by the extent to which each of the personality disorders shares traits of the FFM (Lynam & Widiger, 2001; O'Connor, 2005).

Proposed for *DSM-5* was a five-domain 25-trait dimensional model that represented "maladaptive variants of the five domains of the extensively validated and replicated personality model known as the 'Big Five,' or the Five Factor Model of personality" (APA, 2013, p. 773). These five domains are negative affectivity (FFM neuroticism), detachment (FFM introversion), psychoticism (FFM openness), antagonism (FFM antagonism), and disinhibition (low FFM conscientiousness). The *DSM-5* dimensional trait model does differ in important ways from the FFM; more specifically, it is confined to maladaptive personality functioning and it is unipolar in structure (e.g., it does not recognize any maladaptive variants of extraversion that is opposite to detachment, or agreeableness that is opposite to antagonism). Nevertheless, there is strong conceptual and empirical support for its alignment with the five domains of the FFM (APA, 2013; De Fruyt, De Clerq, De Bolle, Markon, & Krueger, 2013; Gore & Widiger, 2013; Thomas et al., 2013; Widiger, 2011).

The FFM of personality disorder has a number of advantages over the existing categorical approach (Widiger et al., 2012). It would help with the stigmatization of a personality disorder diagnosis because no longer would a personality disorder be conceptualized as something that is qualitatively distinct from general personality traits. All persons vary in the extent of their neuroticism, in the extent to which they are agreeable versus antagonistic, and in the extent to which they are conscientious, impulsive, and/or undependable (McCrae & Costa, 2003). The FFM of personality disorder will provide not only a more precise description of each person's individual personality structure but will also provide a more complete picture through the inclusion of normal, adaptive traits, recognizing thereby that a person is more than just the personality disorder and that there are aspects to the self that can be adaptive, even commendable, despite the presence of the maladaptive personality traits. Some of the personality strengths may also be quite relevant to treatment, such as openness to experience, indicating an interest in exploratory psychotherapy; agreeableness, indicating an engagement in group therapy; and conscientiousness, indicating a willingness and ability to adhere to the demands and rigor of dialectical behavior therapy (Sanderson & Clarkin, 2002). The FFM of personality disorder would also bring to the psychiatric nomenclature a wealth of knowledge concerning the origins, childhood antecedents, stability, and universality of the dispositions that underlie personality disorder (Widiger et al., 2012; Widiger & Trull, 2007).

The Nomenclature Work Group at the initial *DSM-5* Research Planning Conference called for the replacement of the *DSM-IV-TR* diagnostic categories by a dimensional model (Rounsaville et al., 2002). "If a dimensional system of personality performs well and is acceptable to clinicians, it might then be appropriate to explore dimensional approaches in other domains" (Rounsaville et al., 2002, p. 13). A subsequent APA *DSM-5* preparatory conference was devoted to making this shift, providing its extensive empirical support (Widiger et al., 2005). The proposal of the DSM-5 Personality and Personality Disorders Work Group though was more conservative. The proposal was not to replace the diagnostic categories with a dimensional trait model. It was only to provide a dimensional trait model as a

supplement for the existing diagnostic categories, although the traits would be part of the criterion sets for these categories (Skodol, 2012). Nevertheless, this more conservative proposal was still rejected, for reasons that are not clear. It is true that the initial dimensional trait proposal had been created de novo by work group members, thereby lacking a strong empirical foundation. In addition, rather than closely tying the proposal to the FFM, the authors explicitly distanced the proposal from the FFM (Clark & Krueger, 2010). In the last year of the proposal it was more closely tied to the FFM (APA, 2012) but by then strong opposition to the proposal had accumulated (Gunderson, 2010; Shedler et al., 2010). In addition, it was also structurally embedded within a much more extensive and complex proposal that included additional features of personality disorder concerning self pathology derived from psychodynamic theory and research (Skodol, 2012). Nevertheless, it is at least included in Section 3 of *DSM-5* for emerging measures and models as an alternative to the *DSM-5* diagnostic categories that have been carried over from *DSM-IV-TR* categories without any revision.

Intellectual Disability

Rounsaville et al. (2002) and others suggested that the personality disorders section be the first to shift toward a dimensional classification, apparently not fully appreciating that one section has long been dimensional: intellectual disability (previously called mental retardation). Many persons write as if a shift to a dimensional classification represents a new, fundamental change to the diagnostic manual (e.g., Regier, 2008). For much of the manual such a shift would certainly represent a fundamental change in how mental disorders are conceptualized and classified (Guze, 1978; Guze & Helzer, 1987; Robins & Guze, 1970). Nevertheless, there is a clear precedent for a dimensional classification of psychopathology already included within *DSM-5:* the diagnosis of intellectual disability (APA, 2013).

Intellectual disability in *DSM-5* is diagnosed along a continuum of cognitive and social functioning; more precisely, deficits in adaptive functioning and intellectual functions confirmed by standardized intelligence testing. This typically translates to an intelligence quotient score of 70, plus or minus 5 (APA, 2013). An IQ of 70 does not carve nature at a discrete joint or identify the presence of a qualitatively distinct condition, disease, or disorder. On the contrary, it is a quantitative cutoff point along the dimension of intelligence. An IQ of 70 is simply two standard deviations below the mean (American Association of Mental Retardation [AAMR], 2002).

Intelligence involves the ability to reason, plan, solve problems, think abstractly, comprehend complex ideas, learn quickly, and learn from experience (AAMR, 2002). Intelligence, like personality, is distributed as a hierarchical, multifactorial continuous variable. Most persons' levels of intelligence, including most of those with an intellectual disability, are the result of a complex interaction of multiple genetic, fetal, and infant development, and environmental influences (Deary, Spinath, & Bates, 2006). There are no discrete breaks in its distribution that would provide an absolute distinction between normal and abnormal intelligence. The point of demarcation for the diagnosis of an intellectual disability is an arbitrary, quantitative distinction along the normally distributed levels of hierarchically and multifactorially defined intelligence. This point of demarcation is arbitrary in the sense that it does not carve nature

at a discrete joint, but it was not, of course, randomly or mindlessly chosen. It is a defensible selection that was informed by the impairments in adaptive functioning commonly associated with an IQ of 70 or below (AAMR, 2002). For example, a previous cutoff point of an IQ of 79 identified too many persons who were in fact able to function independently.

In addition, the disorder of intellectual disability is not diagnosed simply on the basis of an IQ of 70 or below (an IQ score is not even necessarily required in *DSM-5*; APA, 2013). It must be accompanied by a documented impairment to functioning. "Mental retardation is a disability characterized by significant limitation in both intellectual functioning and in adaptive behavior as expressed in conceptual, social and practical adaptive skills" (AAMR, 2002, p. 23). Persons with IQ scores lower than 70 who can function effectively would not be diagnosed with the disorder (APA, 2013). The diagnosis is understood in the context of the social and practical requirements of everyday functioning that must be met by the person (Luckasson & Reeve, 2001). The purpose of the diagnosis is not to suggest that a specific pathology is present, but to identify persons who, on the basis of their intellectual disability, would be eligible for public health-care services and benefits to help them overcome or compensate for their relatively lower levels of intelligence.

Many instances of intellectual disability are due in large part to specific etiologies, such as tuberous sclerosis, microcephaly, von Recklinghausen's disease, Trisomy 21, Mosaicism, Prader-Willi syndrome, and many, many more (Kendell & Jablensky, 2003). Nevertheless, the disorders that result from these specific etiologies are generally understood as medical conditions, an associated feature of which is also the intellectual disability that would be diagnosed concurrently and independently. The intellectual disability that is diagnosed as a mental disorder within *DSM-5* is itself a multifactorially determined and heterogeneous dimensional construct falling along the broad continuum of intellectual functioning. "The causes of intellectual disabilities are typically complex interactions of biological, behavioral/psychological, and sociocultural factors" (Naglieri, Salter, & Rojahn, 2008, p. 409). An important postnatal cause for intellectual disability is "simply" psychosocial deprivation, resulting from poverty, chaotic living environment, and/or child abuse or neglect. No clear etiology will be evident in up to 40% of cases. In sum, intellectual disability may serve as an effective model for the classification of the rest of the diagnostic manual, including mood, psychotic, personality, anxiety, and other mental disorders.

DSM-5 AND DIMENSIONAL CLASSIFICATION

The modern effort to demarcate a taxonomy of distinct clinical conditions is often traced to Kraepelin (1917). Kraepelin (1917), however, had himself acknowledged, "wherever we try to mark out the frontier between mental health and disease, we find a neutral territory, in which the imperceptible change from the realm of normal life to that of obvious derangement takes place" (p. 295). The Robins and Guze (1970) paradigm for the validation of categorical diagnosis has also been widely influential within psychiatry (Klerman, 1983; Kupfer et al., 2002). In 1989, L. Robins and Barrett (1989) edited a text in honor of this classic paper. Kendell (1989) provided the final word in his closing chapter. His conclusions, however, were curiously negative.

"Ninety years have now elapsed since Kraepelin first provided the framework of a plausible classification of mental disorders. Why then, with so many potential validators available, have we made so little progress since that time?" (Kendell, 1989, p. 313). He answered his rhetorical question in the next paragraph: "One important possibility is that the discrete clusters of psychiatric symptoms we are trying to delineate do not actually exist but are as much a mirage as discrete personality types" (Kendell, 1989, p. 313).

It is stated in the preface to *DSM-5* that "this edition of *DSM* was designed first and foremost to be a useful guide to clinical practice" (APA, 2013, p. xii). First (2005) argued in his rejoinder to a proposal to shift the diagnostic manual into a dimension model, that "the most important obstacle standing in the way of its implementation in *DSM-5* (and beyond) is questions about clinical utility" (p. 561). However, one should question whether the existing diagnostic manual in fact has appreciable clinical utility (Mullins-Sweatt & Widiger, 2009). "Apologists for categorical diagnoses argue that the system has clinical utility being easy to use and valuable in formulating cases and planning treatment [but] there is little evidence for these assertions" (Livesley, 2001a, p. 278). First (2005) suggested that "the current categorical system of *DSM* has clinical utility with regard to the treatment of individuals" (p. 562), yet elsewhere has stated that "with regard to treatment, lack of treatment specificity is the rule rather than the exception" (Kupfer et al., 2002, p. xviii). The heterogeneity of diagnostic membership, the lack of precision in description, the excessive diagnostic co-occurrence, the failure to lead to a specific diagnosis, the reliance on the "not otherwise specified" waste-basket diagnosis, and the unstable and arbitrary diagnostic boundaries of the *DSM-IV-TR* and *DSM-5* categories, are matters of clinical utility that is a source of considerable frustration for clinicians and public health care agencies (Mullins-Sweatt & Widiger, 2009).

The primary goal of the authors of *DSM-5* was to shift the manual toward a dimensional classification (Helzer, Wittchen, Krueger, & Kraemer, 2008; Regier, Narrow, Kuhl, & Kupfer, 2010). This intention represented an explicit recognition of the failure of the categorical system (D. Goldberg, 2010). And, DSM-5 does indeed include a number of clear and potentially significant shifts toward a dimensional classification. The introduction to the manual explicitly acknowledges the failure of the categorical model: "The once plausible goal of identifying homogeneous populations for treatment and research resulted in narrow diagnostic categories that did not capture clinical reality, symptom heterogeneity within disorders, and significant sharing of symptoms across multiple disorders" (APA, 2013, p. 12). It is further asserted that dimensional approaches will "supersede current categorical approaches in coming years" (p. 13). In addition, many of the changes that were made to the nomenclature reflected a preference for a more dimensional conceptualization (e.g., the autism spectrum disorder, the conceptualization of a schizophrenia spectrum, the level of severity for substance use disorder, and the reference within the introduction of the manual to the broad dimensions of internalizing and externalizing dysfunction that cut across existing categories). Included in Section 3 of *DSM-5* for emerging models and measures is a five-domain 25-trait dimensional model of maladaptive personality functioning (Krueger et al., 2011) that is aligned conceptually and empirically with the FFM dimensional model of general personality structure (APA, 2013; De Fruyt et al., 2013; Gore & Widiger, 2013; Thomas et al.,

2013). This model is presented as an alternative to the traditional diagnostic categories "to address numerous shortcomings of the current approach" (APA, 2013, p. 761) and its presence within the diagnostic manual will help stimulate further research as well as increase the familiarity and interest of clinicians with respect to this alternative approach (Widiger, 2013).

Nevertheless, it is also acknowledged that "DSM-5 remains a categorical classification of separate disorders" (APA, 2013, p. xii). The shifts that did occur were frankly tentative, if not timid. "What is being proposed for DSM-V is not to substitute dimensional scales for categorical diagnoses, but to add a dimensional option to the usual categorical diagnoses for DSM-V" (Kraemer, 2008, p. 9). None of the mental disorders, including even the personality disorders, converted to a dimensional classification. There was a shift toward the conceptualization of some disorders as existing along a spectrum (e.g., autism and schizophrenia), and substance use disorder collapsed the problematic distinction between abuse and dependence into one disorder that includes four levels of severity. However, with respect to the latter, there remains no acknowledgement of the continuum into normal substance usage. There will continue to be a reliance on the NOS category to identify subthreshold conditions (the threshold for a substance use diagnosis was, in fact, raised from one criterion to two).

DSM-III is often said to have provided a significant paradigm shift in how psychopathology is diagnosed (Kendell & Jablensky, 2003; Klerman, 1983; Regier, 2008). Much of the credit for the innovative nature and success of *DSM-III* is due to the foresight, resolve, and perhaps even courage of its Chair, Dr. Robert Spitzer. The primary authors of *DSM-5* fully recognized the failure of the categorical model of classification (Kupfer et al., 2002; Regier, 2008; Regier et al., 2010). They had the empirical support and the opportunity to lead the field of psychiatry to a comparably bold new future in diagnosis and classification, but no true paradigm shift in the classification of psychopathology has occurred.

There was never an intention though to actually shift the diagnostic manual into a dimensional system. As acknowledged by Helzer, Kraemer, and Krueger (2006), "our proposal [for *DSM-5*] not only preserves categorical definitions but also does not alter the process by which these definitions would be developed. Those charged with developing criteria for specific mental disorders would operate just as their predecessors have" (p. 1675). In other words, work groups, for the most part, continued to develop diagnostic criteria to describe prototypic cases in a manner that would maximize homogeneity and differential diagnosis (Robins & Guze, 1970; Spitzer et al., 1980), thereby continuing to fail to adequately describe typical cases and again leaving many patients to receive the diagnosis of NOS. Dimensional proposals for *DSM-5* were only to develop "supplementary dimensional approaches to the categorical definitions that would also relate back to the categorical definitions" (Helzer, Wittchen, et al., 2008, p. 116). It was the intention for these dimensions to only serve as ancillary descriptions that lacked any official representation within a patient's medical record. They have no official alphanumerical code and may then not even be communicated to any public health care agency.

Kraemer, Noda, and O'Hara (2004) argued that in psychiatry "a categorical diagnosis is necessary" (p. 21). "Clinicians who must decide whether to treat or not treat a patient, to hospitalize or not, to treat a patient with a drug or with

psychotherapy, or what type, must inevitably use a categorical approach to diagnosis" (Kraemer et al., 2004, p. 12). This is a not uncommon perception, but it is not an accurate characterization of actual clinical practice (Mullins-Sweatt & Widiger, 2009). In many common clinical situations, the decision is not in fact black and white. Clinicians and social agencies make decisions with respect to a frequency of therapy sessions, an extent of insurance coverage, a degree of medication dosage, and even degrees of hospitalization (e.g., day hospital, partial hospitalization, residential program, or traditional hospitalization).

It is evident that these different clinical decisions are not well informed by a single, uniform diagnostic threshold. The current diagnostic thresholds are not set at a point that is optimal for any one particular social or clinical decision, and the single diagnostic threshold is used to inform a wide variety of different decisions. A dimensional system has the flexibility to provide different thresholds for different social and clinical decisions and would then be considerably more useful for clinicians and more credible for social agencies than the current system. A flexible (dimensional) classification would be preferable to governmental, social, and professional agencies because it would provide a more reliable, valid, explicitly defined, and tailored means for making each respective social and clinical concern. It is for this reason that the authors of *DSM-5* included the supplementary dimensional scales to facilitate particular clinical decisions (e.g., Shear, Bjelland, Beesdo, Gloster, & Wittchen, 2008).

The National Institute of Mental Health (NIMH) has largely rejected *DSM-5*, indicating that they are no longer interested in funding studies that rely upon this nomenclature. As expressed by the director of NIMH, "it is critical to realize that we cannot succeed if we use DSM categories" (Insel, 2013). NIMH has developed its own nomenclature, referred to as the Research Domain Criteria (RdoC; Insel, 2009; Sanislow et al., 2010), consisting of five broad areas of research (i.e., negative valence systems, positive valence systems, cognitive systems, systems for social processes, and arousal/modulatory systems) that cut across the existing *DSM-5* diagnoses. The RDoC nomenclature is described as dimensional, because it is concerned with underlying mechanisms that are best described in terms of levels or degrees of functioning rather than distinct categories. "Each level of analysis needs to be understood across a dimension of function" (Insel, 2013). However, the primary distinction with *DSM-5* is that the RDoC system emphasizes a neurobiological model of psychopathology. "Mental disorders are biological disorders involving brain circuits that implicate specific domains of cognition, emotion, or behavior" (Insel, 2013). NIMH is primarily critical of the *DSM-5* for deriving its diagnoses on the basis of overt symptoms (Craddock & Owen, 2010; Kapur, Phillips, & Insel, 2012). "Unlike our definitions of ischemic heart disease, lymphoma, or AIDS, the *DSM* diagnoses are based on a consensus about clusters of clinical symptoms, not any objective laboratory measure" (Insel, 2013). However, it is also unclear if a biological reductionism will be any more successful (Kendler, 2005).

Most (if not all) mental disorders appear to be the result of a complex interaction of an array of interacting biological vulnerabilities and dispositions with a number of significant environmental, psychosocial events that often exert their effects over a progressively developing period of time (Rutter, 2003). The most complete and compelling explanation will not likely be achieved through a biological reductionism because much will be lost by a failure to appreciate that explanation and

understanding at the level of behavior and cognition remains fundamentally valid, and necessary (Kendler, 2005). The symptoms and pathologies of mental disorders appear to be highly responsive to a wide variety of neurobiological, interpersonal, cognitive, and other mediating and moderating variables that help to develop, shape, and form a particular individual's psychopathology profile. This complex etiological history and individual psychopathology profile are unlikely to be well described by single diagnostic categories that attempt to make distinctions at nonexistent discrete joints along the continuous distributions (Widiger & Samuel, 2005). The publication of *DSM-III* was said to have provided a significant, major advance in the diagnosis and classification of psychopathology (Klerman, 1983). The APA diagnostic nomenclature, however, is now beset by substantial criticism (Frances, 2013; Greenberg, 2013), with NIMH openly rejecting it (Insel, 2013). Perhaps it is time for a paradigm shift.

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CHAPTER 2

The Problem of Dual Diagnosis

MELANIE E. BENNETT, JASON PEER, and SELVIJA GJONBALAJ-MAROVIC

RESEARCH INDICATES THAT a substantial percentage of the general population with a lifetime psychiatric disorder has a history of some other disorder (Kessler, 1997; Kessler et al., 1994), and more than half of patients in psychiatric treatment meet criteria for more than one diagnosis (Wolf, Schubert, Patterson, Marion, & Grande, 1988). The issue of comorbidity broadly refers to combinations of any types of psychiatric disorders that co-occur in the same individual. A diagnostic pair that has received significant attention over the past two decades is that of mental illness and substance abuse. The term *dual diagnosis* describes individuals who meet diagnostic criteria for an Axis I or Axis II mental disorder (or disorders) along with one or more substance use disorders. Although dual diagnosis has likely been a prevalent and persistent condition for a long time, it began to receive attention as both a clinical problem and research domain some 25 years ago. Today, we find ourselves with many years of research and thinking about the frequent association between mental and substance use disorders, how this association complicates the provision of mental health and substance abuse treatment services, and the impact of this association on all aspects of psychopathology research and clinical practice. In this chapter, we review data on rates of dual diagnosis, both generally and for specific domains of disorders, as well as discuss some of the ways in which dual diagnosis impacts the course, prognosis, assessment, and treatment of adult psychopathology. Finally, we review current research and thinking on the etiology of dual diagnosis and highlight clinical and research directions.

A recurring theme throughout this chapter is the many ways that the conceptualization of dual diagnosis can change depending on definitions, diagnostic frameworks, assessment tools, and the sample being evaluated. Over time and as these domains have changed, thinking about what mental health and substance use disorders should be included within the conceptualization of dual diagnosis, as well as how to think about the impact of dual diagnosis on outcomes, has evolved and shifted. Our goal here is to review the literature on dual diagnosis, to present ideas that can challenge and perhaps expand the thinking on what constitutes dual

diagnosis, and to provide consideration of how such expansion may impact thinking on psychopathology and diagnosis.

METHODOLOGICAL ISSUES IN THE ASSESSMENT OF DUAL DIAGNOSIS

There are several methodological issues to consider when reviewing the literature on dual diagnosis and evaluating its findings. These include the way that the sample under study shapes the findings, the range of methods used to assess psychiatric and substance use disorders and how different methods and measures shape study findings, and the critical impact of one's definition of dual diagnosis on study findings.

Sample Selection Influences Findings

Data on the epidemiology of dual diagnosis come from both epidemiological and clinical studies, each of which has benefits and drawbacks. Several large-scale epidemiological studies examining rates of dual diagnosis in general population samples have been carried out since the mid-1980s. These studies provide representative information on rates of mental illness and substance use disorders, use structured diagnostic interviews, and generate results that are reliable and relevant to the population as a whole. Most of the information on rates of dual diagnosis comes from studies of clinical populations. Although such studies are not representative of the general population, they provide valuable information on the types of problems that are faced by individuals in treatment, as well as on the links between dual diagnosis, service utilization, the impact on illness, and treatment outcome. Importantly, individuals with multiple disorders are more likely to seek treatment, a condition known as Berkson's fallacy (Berkson, 1949), so that estimates of the prevalence of comorbid disorders will be higher in clinical samples. Relatedly, factors such as inpatient or outpatient status and chronicity of illness may affect rates of dual diagnosis found in clinical samples. For example, research on patients with schizophrenia has found that more severely impaired inpatients are less likely to abuse substances than patients who are less ill (Mueser et al., 1990). Dual diagnosis rates have also been found to differ by setting, with hospital emergency rooms reflecting higher estimates than other settings (Barbee, Clark, Crapanzano, Heintz, & Kehoe, 1989; Galanter, Castaneda, & Ferman, 1988). In addition, several demographic variables correlate with substance abuse, and differences in these variables in clinical samples can influence prevalence rates. For example, gender and age both correlate with substance abuse: Males and those of younger age are more likely to abuse substances. Because studies of comorbidity in schizophrenia often use samples of inpatients who are more likely to be male, the comorbidity rate in schizophrenia found in research with clinical samples may be inflated, because males are both more likely to have substance use disorders and more likely to be inpatients in psychiatric hospitals.

Another sample-related methodological issue involves the split between the mental health treatment system and the substance abuse treatment system, and the impact that this separation has on dual diagnosis research. The literature on dual diagnosis really includes two largely separate areas of investigation: research on substance abuse in individuals with mental illness, and research on mental illness in primary

substance abusers. In order to get an accurate picture of dual diagnosis and its full impact on clinical functioning and research in psychopathology, both aspects of this literature must be examined.

Study Methods and Assessment Measures Influence Findings

The methods used to determine psychiatric and substance use diagnoses can influence findings. The types of diagnostic measures used include structured research interviews, nonstructured clinical interviews, self-report ratings, and reviews of medical records. Although structured interviews are the most reliable method of diagnosis (Mueser, Bellack, & Blanchard, 1992), research with clinical samples will often employ less well-standardized assessments. Relatedly, studies measure different substances in their assessments of dual diagnosis, typically including alcohol, cocaine, heroin, hallucinogens, stimulants, and marijuana. Importantly, some substances are not typically considered in assessments of dual diagnosis. For example, nicotine is usually not considered a substance of abuse in dual diagnosis research, despite the high rates of use among individuals with both mental illness (Lasser et al., 2000) and substance abuse (Bien & Burge, 1990), as well as a growing literature that suggests that nicotine dependence has links, perhaps biological in nature, to both major depression (Quattrocki, Baird, & Yurgelun-Todd, 2000) and schizophrenia (Dalack & Meador-Woodruff, 1996; Ziedonis & George, 1997). Others have found elevated rates of psychiatric and substance use disorders in smokers (Keuthen et al., 2000). Taken together, factors such as the type of problematic substance use assessed, the measures that are used, and the specific substances that are included in an assessment all contribute to varying meanings of the term *dual diagnosis*.

There Is No Single Definition of Dual Diagnosis

Definitions of what constitutes dual diagnosis are far from uniform. Studies often use differing definitions and measures of substance use disorders, making prevalence rates diverse and difficult to compare. For example, definitions used to determine rates of dual diagnosis vary, ranging from problem use of a substance based on the frequency of use or the number of negative consequences experienced as a result of use, to abuse or dependence based on formal diagnostic criteria. This is a particularly important issue when formal diagnostic criteria for substance use disorders are used to assess dual diagnosis.

Currently the two most widely used systems for psychiatric diagnosis and classification are the *Diagnostic and Statistical Manual* (*DSM*; American Psychiatric Association [APA], 1994), used primarily in the United States, and the *International Classification of Diseases* (*ICD*) (World Health Organization [WHO], 1993), used primarily in other countries. There are several issues related to these diagnostic frameworks that are must be considered. Having different systems internationally means that studies done in different countries will use different definitions of psychiatric and substance use disorders, presenting a challenge when making comparisons across studies.

Importantly, these diagnostic systems are similar but not identical, and there are important features of each that influence how substance use disorders are diagnosed

that can, in turn, influence rates of dual disorders. The diagnostic criteria for alcohol use disorders from the fourth edition of *DSM (DSM-IV)* and the 10th edition of the *ICD (ICD-10)* provide a good example (see Hasin, 2003, for a complete review). Both systems include a diagnosis of alcohol dependence that requires at least three symptoms be present from a list of six (*ICD-10*) or seven (*DSM-IV*) that include both physiological symptoms such as tolerance and withdrawal as well as non-physiological symptoms such as impaired control, giving up other important activities, and continued use in the face of physical or psychological consequences.

Research has shown good reliability between *DSM* and *ICD* for dependence diagnoses (Hasin, 2003). In contrast, these systems differ with respect to diagnoses of alcohol abuse (as it is called in *DSM-IV*) or harmful use (as found in *ICD-10*). *DSM-IV* requires "recurrent use" that leads to at least one of four possible consequences (failure to fulfill obligations, use in situations in which it is physically hazardous, use-related legal problems, use despite recurrent social/interpersonal problems) in order to meet a diagnosis of alcohol abuse. *ICD-10* is more specific in its definition of "recurrent" ("The pattern of use has persisted for at least 1 month or has occurred repeatedly within a 12-month period") but less specific in describing those consequences that are "harmful," requiring only "clear evidence that alcohol use contributed to physical or psychological harm" and that a "pattern of use has persisted" (WHO, 1993). Such differences in criteria have no doubt contributed to findings of lower reliability between these categories (Hasin, 2003). Moreover, these sorts of differences are especially important when considering how rates of dual disorders compare across nations and cultures (see Room, 2006, for a review).

Another critical consideration is that both *DSM* and the *ICD* are changing systems. The preceding example was based on diagnostic criteria found in *DSM-IV* and *ICD-10*. However, in May 2013, a new edition of *DSM*, *DSM-5* (APA, 2013), was published, with significant implications for dual diagnosis. *DSM-5* includes new disorders (for example, disruptive mood dysregulation disorder has been added to the chapter on Depressive Disorders), changes to the symptom requirements needed to meet criteria for some disorders (for example, a diagnosis of schizophrenia now requires at least one positive symptom), and consolidation of related conditions into a single diagnostic classification (for example, autistic disorder, Asperger's disorder, childhood disintegrative disorder, and pervasive developmental disorder not otherwise specified have been merged within Autism Spectrum Disorder). Overall, *DSM-5* now has fewer total diagnoses—the revisions yielded 15 new diagnoses, 2 diagnoses that were not continued, and 28 that were combined. These sorts of changes can impact definitions and prevalence rates of dual diagnosis. For example, in *DSM-5*, the bereavement exclusion for major depressive disorder has been eliminated. This has the potential to yield some additional cases of major depression or to identify major depression earlier following loss. Although it is not yet clear how such a change would definitively impact rates of dual diagnosis, it is possible that this change would yield additional cases of major depression that could, in turn, yield more individuals affected by dual diagnosis. As the changes to diagnosis codified in *DSM-5* begin to be used, we will be able to examine whether and how dual diagnosis is impacted.

There were also several changes in the diagnosis of substance use disorders. The title of the chapter dedicated to alcohol and drug diagnoses was revised from

Substance Use Disorders *(DSM-IV)* to Substance-Related and Addictive Disorders *(DSM-5)*; this revision reflects several changes that will have a substantial impact both on how disorders related to alcohol and drug use are diagnosed *and* in the inclusion of other conditions as addictions. To begin with, whereas *DSM-IV* had separate diagnostic groups for substance abuse and dependence, *DSM-5* combines abuse and dependence into one diagnostic category (substance use disorder) that is rated on a continuum from mild to severe, with the severity rating based on the number of criteria met (mild = two to three criteria met; moderate = four to five criteria met; severe = six or more criteria met). There also have been changes to the diagnostic criteria for substance use disorder. For example, the criterion of "recurrent legal problems" that was part of the substance abuse diagnosis in *DSM-IV* was not retained in *DSM-5*, and a new criterion—"craving or a strong desire or urge to use a substance"—was added. In addition, while in *DSM-IV* one or more criteria needed to be met to earn a diagnosis of substance abuse and three or more needed to be met for substance dependence, now in *DSM-5*, a diagnosis of substance use disorder requires that 2 criteria from a list of 11 be met.

These changes will have a substantial impact on dual diagnosis. Combining abuse and dependence into one diagnostic category can have the effect of identifying what might have previously been thought of as a less problematic or separate state (abuse) as a more serious condition that is potentially related to something more serious (dependence), with rates of dual diagnosis increasing as a result. Importantly, the longer list of diagnostic criteria and the severity rating symptom are a visible indication of the thinking that mild substance-related problems are fundamentally related to more severe ones. That is, these are not separate diagnostic categories but ones that are related, different not in the makeup of the conditions but by degree. This pathway from mild to moderate to severe substance use disorder has the potential to impact dual diagnosis by including less severe substance use problems within the dual diagnosis framework. Whereas problem or heavy substance use that did not meet the threshold for a dependence diagnosis previously may not have been considered as part of a definition of dual diagnosis, now less severe expressions of substance use are considered a disorder that would be captured within the definition of dual diagnosis.

The shift from conceptualizing substance use disorders from abuse versus dependence categories to a continuous dimension was informed by a growing literature of psychometric analyses of *DSM-IV* substance use disorder criteria. Studies using traditional factor analysis, latent trait modeling, and item response theory (IRT) analysis all point to a single continuous factor as the most parsimonious representation of substance-abuse and dependence symptom criteria. Specifically, several studies using exploratory factor analysis found that a single factor solution including both abuse and dependence symptoms had the best fit for alcohol use disorders (Borges et al., 2010; Harford, Yi, Faden, & Chen, 2009; Lagenbucher et al., 2004) and marijuana and cocaine use disorders (Lagenbucher et al., 2004). In addition, these findings remained consistent across different national contexts (Borges et al., 2010) and age groups (Harford et al., 2009; Martin, Chung, Kirisci, & Lagenbucher, 2006). Further, studies utilized an analysis of substance use criteria based on IRT and found that the substance abuse and dependence criteria did not fall on a continuum of severity in a manner consistent with the *DSM-IV*

conceptualization of abuse and dependence typology for alcohol use disorders (Borges et al., 2010; Lagenbucher et al., 2004; Harford et al., 2009) and cocaine and marijuana use disorders (Lagenbucher et al., 2004; Martin et al., 2006). Specifically, for each item, IRT quantifies where an item falls on a latent variable representing severity of substance use disorders and the ability of each item to discriminate between subsequent levels of that latent variable.

The *DSM-IV* typology would predict that those individuals with less severe substance use disorders would be less likely to endorse items associated with substance dependence (e.g., those items with greater severity) and that these items would be more closely related with regard to severity. However, when models were specified to order items in such a way, they tended to have poorer fit (Lagenbucher et al., 2004). Finally, these studies have found some evidence that criteria may be interpreted differently by respondents depending on age or national context (Borges et al., 2010; Lagenbucher et al., 2004). In sum, this greater psychometric scrutiny of DSM symptom criteria has led to a reconceptualization of substance use disorders as a continuum and it is likely that similar analysis in the future will lead to greater refinements and precision in diagnostic criteria. In turn, this notion of a continuum from mild to moderate to severe substance use disorder has the potential to impact definitions of dual diagnosis. Where, in the past, substance abuse diagnosis may not have been considered in dual diagnosis, we may now instead need to consider dual diagnosis as a continuous variable as opposed to a categorical one. We may need to consider the correlation between the severity of substance use disorder and specific Axis I diagnostic categories to best understand how different disorders are interrelated or interact with each other.

Another important change in *DSM-5* is expansion of the chapter on substance use disorders to include gambling disorder, based on a body of research that now indicates that many of the same underlying neurobiological processes that are activated and make substance use biologically reinforcing are found in problem gamblers, and that symptoms of problematic gambling are similar in many ways to those of substance use disorders (Petry, 2006). The inclusion of a non-substance-related addiction alongside substance-related ones provides an interesting set of questions. Should gambling disorders now be included in the thinking about dual diagnosis? What does this mean for (the likely increase in) prevalence rates of dual diagnosis that might accompany such a change, our understanding of the causes of dual diagnosis, and implications for assessment and treatment? If the most widely accepted definition of dual diagnosis involves meeting diagnostic criteria for an Axis I or Axis II mental disorder (or disorders) along with one or more substance use disorders, and gambling disorder is fundamentally similar in many ways to alcohol or drug use disorders, does the definition need to be broadened to include non-substance addictions?

The inclusion of gambling disorder in *DSM-5* and the questions this change raises for definitions of dual diagnosis illustrate a broader issue: What one identifies as a diagnosis is key to any definition of dual diagnosis. Gambling provides but one example. Another example can be seen with tobacco dependence. Although there is a large literature documenting higher rates of smoking among individuals with psychiatric disorders (Farrell et al., 2003), tobacco dependence has not traditionally been included as part of the definition of dual diagnosis. This is generally because with such

high rates of smoking among those with psychiatric disorders, including it would yield extremely high rates of dual diagnosis, potentially sapping the concept of its meaning (if everyone has dual diagnosis, does it become less important?). However, with growing evidence that smoking may be related to the neurophysiology of some psychiatric disorders (Wing, Wass, Soh, & George, 2012), it may be that tobacco dependence represents an especially important substance use disorder to include as part of a definition of dual diagnosis. The greater attention to gambling disorder and tobacco dependence illustrates the ways in which changing ideas about mental health problems and addictions can impact rates of dual diagnosis.

A final issue here concerns the definition of dual diagnosis itself. As noted earlier, dual diagnosis has generally been used to describe the co-occurrence within an individual of an Axis I or Axis II mental disorder (or disorders), with one or more substance use disorders. Within this definition lie many combinations of psychiatric and substance use disorders. It is important to keep in mind that the literature on dual diagnosis is, by necessity, simplified and compartmentalized by the definitions used to guide it.

FINDINGS FROM MAJOR EPIDEMIOLOGICAL STUDIES

Over the past 25 years, several large-scale epidemiological studies of mental illness have examined rates of dual diagnosis, including the Epidemiologic Catchment Area Study (ECA; Regier et al., 1990), the National Comorbidity Survey (NCS; Kessler et al., 1994), the National Comorbidity Survey Replication (NCS-R; Kessler & Merikangas, 2004), and the National Longitudinal Alcohol Epidemiology Survey (NLAES; Grant et al., 1994). Although each study differs somewhat from the others in methodology, inclusion/exclusion criteria, and diagnostic categories assessed (see Table 2.1 for a brief description of methods for these studies), we can take several points from this literature that can contribute to our thinking about and understanding of dual diagnosis.

Dual Diagnosis Is Highly Prevalent in Community Samples

First, epidemiological studies consistently show that dual diagnosis is highly prevalent in community samples. Each of these studies finds that people with mental illness are at greatly increased risk of having a co-occurring substance use disorder, and people with a substance use disorder are likewise much more likely to meet criteria for an Axis I mental disorder. For example, the Epidemiologic Catchment Area Study (ECA; Regier et al., 1990) was the first large-scale study of comorbidity of psychiatric and substance use disorders in the general population, and documented high rates of dual diagnosis among both individuals with primary mental disorders and those with primary substance use disorders. Overall, individuals with a lifetime history of a mental illness had an odds ratio of 2.3 for a lifetime history of alcohol use disorder and 4.5 for drug use disorder, a clear illustration of how those with mental illness are at substantially increased risk of having a comorbid substance use diagnosis.

When examined by type of disorder, antisocial personality disorder (ASP) showed the highest comorbidity rate (83.6%), followed by bipolar disorder (60.7%),

Table 2.1
Methods of Several Major Epidemiological Studies on Dual Diagnosis

Study	Years	Methods
ECA (Regier et al., 1990)	1980–1984	Surveyed more than 20,000 adults in five cities across the United States both in the community and in institutions. Trained interviewers used the Diagnostic Interview Schedule to determine *DSM-III* diagnoses. Included affective, anxiety, and schizophrenia-spectrum disorders.
NCS (Kessler et al., 1994)	1990–1992	Assessed 12-month and lifetime prevalence rates for a range of psychiatric disorders in more than 8,000 noninstitutionalized individuals ages 15–54 across 48 states using the Composite International Diagnostic Interview (CIDI) and based on *DSM-III-R* criteria.
NLAES (Grant et al., 1994)	1991–1992	Examined rates of co-occurrence of alcohol and drug use disorders and affective disorders in a general population sample. The NLAES is a household survey of more than 42,000 adults in the United States that utilized diagnostic interviews to assess *DSM-IV* diagnostic criteria for alcohol use disorders.
NCS-R (Kessler & Merikangas, 2004)	2001–2002	Nationally representative face-to-face household survey of more than 9,000 noninstitutionalized people ages 18 years or older. Diagnoses based on *DSM-IV* criteria assessed via CIDI interviews.
NESARC (Grant et al., 2004)	2001–2002	Nationally representative face-to-face survey of 43,093 noninstitutionalized respondents, 18 years of age or older, conducted by NIAAA. *DSM-IV* criteria for substance use disorders and nine independent mood and anxiety disorders were assessed with the Alcohol Use Disorders and Associated Disabilities Interview Schedule-DSM-IV Version (AUDADIS-IV), a structured diagnostic interview administered by lay interviewers.

schizophrenia (47.0%), panic disorder (35.8%), obsessive-compulsive disorder (32.8%), and major depression (27.2%). Further analysis of ECA data (Helzer, Robbins, & McEvoy, 1987) found that men and women with posttraumatic stress disorder (PTSD) were 5 times and 1.4 times more likely, respectively, to have a drug use disorder as were men and women without PTSD. Substantial rates of dual diagnosis were also found in primary substance abusers (Regier et al., 1990). Overall, 37% of individuals with an alcohol disorder and 53% of those with a drug use disorder had comorbid mental illness.

Further analyses (Helzer & Pryzbeck, 1988) found that among those with alcohol use disorders, the strongest association was with ASP (odds ratio = 21.0), followed by mania (OR = 6.2) and schizophrenia (OR = 4.0). Like the ECA study, the NCS and the NLAES found markedly high rates of dual diagnosis. NCS (Kessler et al., 1994) findings showed that respondents with mental illness had at least twice the risk of lifetime alcohol or drug use disorder, with even greater risk for individuals with certain types of mental illnesses. Findings were similar for primary substance abusers: The majority of respondents with an alcohol or drug use disorder had a history of some nonsubstance use psychiatric disorder (Kendler, Davis, & Kessler, 1997; Kessler, 1997). Overall, 56.8% of men and 72.4% of women with alcohol abuse

met diagnostic criteria for at least one psychiatric disorder, as did 78.3% of men and 86.0% of women with alcohol dependence (Kendler et al., 1997). Moreover, 59% of those with a lifetime drug use disorder also met criteria for a lifetime psychiatric disorder (Kessler, 1997). Likewise, the NLAES (Grant et al., 1994; Grant & Harford, 1995) found that, among respondents with major depression, 32.5% met criteria for alcohol dependence during their lifetime, as compared to 11.2% of those without major depression. Those with primary alcohol use disorders were almost 4 times more likely to be diagnosed with lifetime depression, and the associations were even stronger for drug use disorders: Individuals with drug dependence were nearly 7 times more likely than those without drug dependence to report lifetime major depression (see Bucholz, 1999, for a review). Such findings clearly illustrate that rates of dual diagnosis are significant among individuals with mental illness and primary substance abusers, and that many types of psychiatric disorders confer an increased risk of substance use disorder. Overall these studies find that a psychiatric diagnosis yields at least double the risk of a lifetime alcohol or drug use disorder.

High Prevalence Rates of Dual Diagnosis Persist Over Time

A second important feature of rates of dual diagnosis is that they appear to be persistent. Examining how rates persist or change over time is important for several reasons. When the ECA and NCS findings were first published, the findings of high rates of both single and dual disorders were significant because they illustrated the many ways in which the understanding, assessment, and treatment of mental illness and substance use disorders were incomplete. The NCS in particular came under increased scrutiny, given that the rates it found for mental illness were even higher than those found by the ECA. Replications of these studies can demonstrate whether the high rates found in the first studies persist over time. In addition, since the first epidemiologic studies were conducted, *DSM* criteria have changed, leading to questions of how these diagnostic changes might impact illness rates. Finally, seeking treatment for mental distress, as well as use of medications for symptoms of depression and anxiety, are now more widely discussed and accepted than they were 10 to 20 years ago, and it is unclear how changing attitudes might impact rates of dual disorders. Findings from several replications of large epidemiologic studies indicate that even with changes in diagnostic criteria and attitudes about psychological distress, rates of dual disorders remain high. For example, the NCS was recently replicated in the NCS-R. The NCS-R (Kessler & Merikangas, 2004) shared much of the same methodology as the original NCS, repeated many questions from the original survey, and included additional questions to tap *DSM-IV* diagnostic criteria. Conducting these studies 10 years apart allows for an examination of the stability in rates of dual diagnosis, as well as how changes in assessment and diagnostic criteria impact the prevalence of dual diagnosis and other comorbid conditions.

Comparisons of data from both studies illustrate the persistent nature of dual diagnosis. That is, although specific values have changed from one interview to another, the overall picture of dual diagnosis remains the same: Prevalence rates are high, and people with mental illness remain at greatly increased risk for developing substance use disorders. For example, for major depressive disorder (MDD; Kessler

et al., 1996) found that 38.6% of respondents who met criteria for lifetime MDD also had a diagnosis of substance use disorder based on NCS data, whereas 18.5% of respondents who met criteria for 12-month MDD also had a diagnosis of substance use disorder. Results from the NCS-R confirmed the high prevalence rates of dual diagnosis in people with MDD: 24.0% of those with lifetime MDD also met criteria for a substance use disorder, and 27.1% of those who met criteria for 12-month MDD also met criteria for a substance use disorder (Kessler, Berglund, et al., 2005). Although the exact percentages change over time, the rates for dual MDD and substance use diagnoses remain strikingly high over the 10 years between studies.

Similar comparisons can be made between the NLAES and a more recent NIAAA survey called the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; Grant et al., 2004). The NESARC stressed the need to ensure that diagnoses of mood and anxiety disorders were independent from substance use disorders. A comparison of the two studies shows that dual mood/anxiety and substance use disorders continue to be highly prevalent in community samples. For example, in the NLAES (Grant & Harford, 1995), respondents with a past-year diagnosis of major depression had a 21.36% rate of a co-occurring alcohol use disorder, compared with 6.92% of those without 12-month major depression (OR = 3.65). Similarly, high odds ratios were found for 12-month major depression and drug use disorders (Grant, 1995).

Importantly, results of the NESARC confirm the persistent association of substance use disorders and affective disorders. People who met criteria for any 12-month mood disorder were 4.5 times more likely to meet criteria for substance dependence (range of 3.4 to 6.4 for the four mood disorders assessed). People who met criteria for any 12-month anxiety disorder were 2.8 times more likely to meet substance dependence criteria (range of 2.2 to 4.2 for the five anxiety disorders assessed). Examining the results in terms of prevalence rates is similar: 19.97% of those with any 12-month mood disorder had at least one substance use disorder (SUD), and 14.96% of those with any 12-month anxiety disorder had at least one SUD. Similarly, 19.67% of those with a 12-month SUD had at least one mood disorder, and 17.71% had at least one anxiety disorder. Overall, comparisons from replications of large epidemiologic studies illustrate the persistence of dual diagnosis over time.

DUAL DIAGNOSIS IS ONLY ONE PART OF THE COMORBIDITY PUZZLE

A third issue that is highlighted in some epidemiological studies is the fact that the term and typical understanding of dual diagnosis may not accurately reflect the nature and complexity of the problem of co-occurring mental and SUDs. That is, co-occurring disorders can take many forms, and limiting attention to a particular number or combination of problems may restrict what we can learn about the links and interactions between mental illness and SUDs. As discussed previously, the term *dual diagnosis* has most often been used to refer to a combination of one mental illness and one SUD. However, epidemiologic studies find high prevalence rates of three or more co-occurring disorders that include but are not limited to dual mental-SUD combinations. For example, Kessler and colleagues (1994) found that 14% of the NCS sample met criteria for three or more comorbid *DSM* disorders, and that these respondents accounted for well over half of the lifetime and 12-month diagnoses

found in the sample. Moreover, these respondents accounted for 89.5% of the severe 12-month disorders, which included active mania, nonaffective psychosis, or other disorders requiring hospitalization or associated with severe role impairment.

Other data from the NCS (Kessler et al., 1996) showed that 31.9% of respondents with lifetime MDD and 18.5% of those with 12-month MDD met criteria for three or more comorbid conditions. In the NCS-R, Kessler, Berglund, et al. (2005) found that 17.3% of respondents met criteria for three or more lifetime disorders. In addition, in examining projected lifetime risk of developing different *DSM* disorders, these authors reported that 80% of projected new onsets were estimated to occur in people who already had disorders. In examining 12-month disorders in the NCS-R sample, Kessler, Chiu, et al. (2005) found similar results: 23% of the sample met criteria for three or more diagnoses. As these authors state, "Although mental disorders are widespread, serious cases are concentrated among a relatively small proportion of cases with high comorbidity" (Kessler, Chiu, et al., 2005, p. 617). Taken together, these findings illustrate the importance of thinking about dual diagnosis in the context of the broader picture of comorbid conditions. People with dual mental and substance use disorders may in fact meet criteria for a combination of multiple mental and substance use disorders.

Such aggregation of mental and SUDs in a small proportion of people should influence conceptualizations regarding the processes underlying dual and comorbid conditions. In addition, comorbidity appears to be influenced by severity of mental illness. Using data from the NCS-R, Kessler and colleagues (2003) examined differences in rates of comorbid disorders (including but not limited to SUDs) in respondents with MDD of differing levels of severity. Specifically, respondents who met criteria for 12-month MDD were classified as showing mild, moderate, severe, or very severe symptoms, based on scores on the Quick Inventory of Depressive Symptomatology Self Report (QIDS-SR) for the worst month in the past year. As severity level increased, so did rates of comorbidity, defined as the percentage of respondents with two or more comorbid 12-month disorders, including SUDs. Specifically, 34.9% of mild, 58.0% of moderate, 77.3% of severe, and 82.1% of very severe MDD cases met criteria for two or more comorbid disorders. This finding of increased severity as number of disorders increases was also found for 12-month diagnoses (Kessler, Chiu, et al., 2005). This trend is another reminder that dual diagnosis and comorbidity labels represent heterogeneous groups of people who differ in meaningful ways that likely have significance in terms of assessment, treatment, and etiology of mental and SUDs.

In sum, epidemiological studies are now able to tell us not only that dual diagnosis is highly prevalent but also that rates of dual disorders persist over time. In addition, we now have ample evidence to suggest that talking about dual disorders is actually a simplification of a complex problem in that patients often have more than two psychiatric disorders as well as use, abuse, or are dependent on multiple substances. Such findings suggest that thinking about the causes of dual disorders may need to be broadened in order to be able to explain this range of diversity among dual-disordered patients.

The Concept of Dual Diagnosis Has Expanded and Changed

As noted earlier, how studies define dual diagnosis has a major impact on prevalence rates. In this section we review three developments that have had an important impact

on prevalence rates of dual diagnosis: including tobacco dependence when defining dual diagnosis, cross-national epidemiological studies, and examination of general population data focused on specific demographic subgroups.

Tobacco Dependence Tobacco is the most widely used substance of abuse among individuals with mental health diagnoses (Farrell et al., 2003) and rates of smoking for individuals with mental health disorders are 2 to 3 times higher what is found in the general population (Lawrence, Mitrou, & Zubrick, 2009). Smokers with mental health disorders have longer smoking histories and, importantly, are less likely to quit: Whereas tobacco use and dependence has been on the decline in the general population, rates have generally remained stable among smokers with mental health disorders (Dickerson et al., 2012; Secades-Villa et al., 2013; Williams, Steinberg, Griffiths, & Cooperman, 2013).

Despite these high prevalence rates, tobacco dependence has not often been considered in research and thinking about dual diagnosis. There are several reasons for this. First, with such high rates of prevalence of tobacco dependence among those with mental health disorders, including tobacco dependence would serve to define a great number of people with a mental health disorder as having a dual diagnosis. Second, there is a complicated history of tolerance and even encouragement of smoking among those with mental health disorders, as many treatment providers believed that individuals would experience symptom relapse or display increased disruptive behavior if not able to smoke, ideas that have since been found to be untrue (el-Guebaly, Cathcart, Currie, Brown, & Gloster, 2002). Third, in the past, tobacco dependence was not fully considered an addiction in the same way that chronic and harmful use of alcohol or illicit drugs was seen. Indeed, for a long time, rates of smoking in the general population were similarly high and the negative consequences of smoking, because they were often far removed from the time of the actual behavior (i.e., the health effects were more likely to manifest after many years of smoking), were not thought about in the same way as the consequences of disordered drinking or illicit drug use.

There are now a range of reasons to consider tobacco dependence when thinking about and studying dual diagnosis. The addictive nature of tobacco/nicotine is now widely known, and the negative health effects of tobacco dependence and other negative consequences for individuals with mental health disorders—cost, stigma, second-hand smoke—have been identified (see Bennett, Wilson, Genderson, & Saperstein, 2013, and Graham, Frost-Pineda, & Gold, 2007 for reviews). As information and knowledge about tobacco dependence has increased, rates of smoking in the general population have decreased dramatically, making tobacco dependence a decreasing problem for many people but still an alarming problem for individuals with mental health disorders. Estimates suggest that individuals with mental health disorders smoke 50% of all cigarettes consumed in this country (Lasser et al., 2000) and that individuals with mental health disorders have a disproportionately difficult time quitting smoking (see Mackowick, Lynch, Weinberger, & George, 2012 for a review). Moreover, research suggests that nicotine may have a unique connection with genetics and brain functioning in some psychiatric disorders including depression and schizophrenia (de Leon & Diaz, 2012; Wing et al., 2012), and that quitting might be more difficult for individuals with mental health disorders due to biological factors that may make smoking more reinforcing (Berg, Sentir, Cooley, Engleman, &

Chambers, 2013) or withdrawal symptoms more problematic (Leventhal, Ameringer, Osborn, Zvolensky, & Langdon, 2013; Weinberger, Desai, & McKee, 2010) than what is experienced by other smokers. For these reasons, we believe a comprehensive review of dual diagnosis should include information on tobacco dependence, and have provided this in the following sections.

The epidemiological studies just listed provide information on rates of tobacco dependence among those with mental health disorders. Lawrence and colleagues (Lawrence et al., 2009) used data from the NCS-R to examine rates of comorbid tobacco dependence and mental health disorders (affective, anxiety, and substance use disorders) as measured by the WHO CIDI. Among respondents with a mental health disorder in the past 12 months, 40.1% were current smokers (almost double the 21.3% smoking prevalence in adults without a mental health disorder in the past 12 months). Rates were highest among those with SUDs (63.6%), followed by individuals with affective disorders (45.1%) and anxiety disorders (37.6%). Goodwin, Zvolensky, Keyes, & Hasin (2012) examined rates of tobacco dependence among those with mental health disorders in the NESARC sample. Diagnoses of specific phobia, personality disorder, major depressive disorder, and bipolar disorder were associated with increased odds of nicotine dependence, as well as with increased risk of persistent nicotine dependence over a 3-year follow-up (Goodwin, Pagura, Spiwak, Lemeshow, & Sareen, 2011). In an examination of associations between smoking and personality disorders using the NESARC sample, Pulay and colleagues (2010) found that the nicotine dependence had the strongest associations with schizotypal, borderline, narcissistic, and obsessive-compulsive personality disorder diagnoses.

Cross-National Epidemiological Studies The preceding review of epidemiological studies focuses on findings from studies conducted in the United States. An interesting and important complement to findings from the United States comes from findings from the WHO World Mental Health Surveys (WMHS; Kessler, Haro, Heeringa, Pennell, & Üstün, 2006), an assessment of diagnosis of mental health disorders using the WHO Composite International Diagnostic Interview (CIDI) carried out in 28 countries around the world with a sample of over 150,000 respondents. Findings from this international survey confirm results from the United States: Mental health disorders are prevalent in all regions of the world, and rates of comorbid SUDs are substantially higher among those with mental health disorders. For example, in an examination of prevalence rates and correlates of bipolar spectrum disorder in a subset of the WHO WMHS sample ($n = 61{,}392$), Merikangas and colleagues (Merikangas et al., 2011) found that 36.6% of those with a bipolar spectrum disorder met criteria for a co-occurring substance use disorder. Other findings from the WHO WMHS replicate findings reviewed above: Comorbidity of multiple mental health disorders, including diagnostic combinations that include psychiatric and SUDs, is associated with greater impairments such as higher risk for suicide (Nock et al., 2009). As more cross-national data are collected and analyzed, it will be important to expand on this work to examine if and how different processes and cultural factors influence the development and persistence of dual diagnosis.

Prevalence of Dual Diagnosis in Older Adults A special population that is important to consider when thinking about dual diagnosis is older adults. With people living

longer, it is important to understand how rates of dual disorders persist or change over time. Findings from the NCS-R show lower rates of diagnosis of mood, anxiety, and substance use disorders for those 65 and older compared to those 18–64 (Gum, King-Kallimanis, & Kohn, 2009). Results from the NESARC (Chou & Cheung, 2013) find that although the overall prevalence of major depressive disorder is low in older adults (2.95% for the past year and 8.82% lifetime), among those with lifetime major depressive disorder, 20% met criteria for an alcohol use disorder.

In line with the idea of including gambling disorder within the definition of dual diagnosis, several studies using NESARC data have found high rates of dual mental and gambling disorders among older adults (Chou & Cheung, 2013; Pilver, Libby, Hoff, & Potenza, 2013), highlighting the way in which older age may impact the traditional definition of dual diagnosis. For example, Pietrzak and colleagues (Pietrzak, Morasco, Blanco, Grant, Petry, 2006) examined over 10,000 older adults in the NESARC survey and found significantly elevated rates of SUDs (alcohol, tobacco, and drugs), as well as mood, anxiety, and personality disorders among those with disordered gambling.

Dual diagnosis may play an important role in a subset of older adults who experience chronic mental health disorders. Mackenzie and colleagues (Mackenzie, El-Gabalawy, Chou, & Sareen, 2013) examined factors that may contribute to persistence of three mental health diagnoses—mood, anxiety, and substance use disorders—over time in older adults surveyed in the NESARC study. Their findings showed that although most disorders were not persistent from one assessment to a second one that was conducted 3 years later, comorbidity of another mental health disorder (including SUDs) was a significant predictor of persistence of any disorder over time.

FINDINGS FROM STUDIES OF CLINICAL SAMPLES

The fact that dual diagnosis is fairly common in the general population serves to highlight the even higher rates found in treatment settings. Clinical studies of dual diagnosis have assessed general psychiatric patients, patients with specific psychiatric disorders, and primary substance abusing patients.

Dual Diagnosis in General Psychiatric Patients

Clinical studies of dual diagnosis over the past 20 years indicate that one-third to three-quarters of general psychiatric patients may meet criteria for comorbid psychiatric and substance use disorders, depending on the diagnostic makeup of the sample and the level of chronicity represented (Ananth et al., 1989; Galanter et al., 1988; McLellan, Druley, & Carson, 1978; Mezzich, Ahn, Fabrega, & Pilkonis, 1990; Safer, 1987). Rates seem to fall in the higher end of this range for samples comprising more impaired patient populations. For example, Ananth and colleagues (1989) found that 72.0% of a sample of patients with schizophrenia, bipolar disorder, and atypical psychosis received a comorbid substance use diagnosis. Mezzich et al. (1990) conducted a large-scale assessment of dual diagnosis in more than 4,000 patients presenting for evaluation and referral for mental health problems over an 18-month period and found substantial rates of dual diagnosis among several diagnostic subsamples. The highest rates were seen among patients with severe mental illnesses

such as bipolar disorder (45% diagnosed with an alcohol use disorder and 39% diagnosed with a drug-use disorder) and schizophrenia or paranoid disorders (42% and 38% were diagnosed with alcohol and other SUDs, respectively). However, dual diagnosis was also pronounced in other patient groups. Specifically, 33% of patients with major depression were diagnosed with an alcohol use disorder, and 18% were diagnosed with a drug use disorder. Among patients with anxiety disorders, 19% and 11% were diagnosed with alcohol and other substance use disorders, respectively.

Dual Diagnosis in Samples of Patients With Specific Disorders

Rates of dual diagnosis have been extensively studied among patients with severe mental illness, including schizophrenia (Dixon, Haas, Weiden, Sweeney, & Frances, 1991; Mueser et al., 1990), bipolar disorder (Bauer et al., 2005; McElroy et al., 2001; Salloum & Thase, 2000; Vieta et al., 2000), and major depression (Goodwin & Jamison, 1990; Lynskey, 1998; Merikangas, Leckman, Prusoff, Pauls, & Weissman, 1985; Swendsen & Merikangas, 2000). Findings show that dual diagnosis is common in such samples. Mueser et al. (1990) evaluated 149 patients with schizophrenia spectrum disorders and found that 47% had a lifetime history of alcohol abuse, whereas many had abused stimulants (25%), cannabis (42%), and hallucinogens (18%). Dixon and colleagues (1991) found that 48% of a sample of schizophrenia patients met criteria for an alcohol or drug use disorder. Chengappa, Levine, Gershon, and Kupfer (2000) evaluated the prevalence of substance abuse and dependence in patients with bipolar disorder.

Among patients with bipolar I, 58% met abuse or dependence criteria for at least one substance, and 11% abused or were dependent on three or more substances. In the bipolar II group, the rate of dual diagnosis was approximately 39%. Baethge and colleagues (2005) followed a group of first-episode bipolar I patients and found that about one-third of the sample had a SUD at the baseline assessment, and that patients using two or more substances showed poorer outcomes over the 2 years of the study. Bauer and colleagues (Bauer et al., 2005) conducted structured interviews with a large sample of inpatient veterans with bipolar disorder across 11 sites ($n = 328$) to examine rates of comorbid anxiety and substance use disorders. Results showed high rates of current (33.8%) and lifetime (72.3%) SUDs in the sample, along with a rate of 29.8% meeting criteria for multiple current disorders.

Hasin, Endicott, and Lewis (1985) examined rates of comorbidity in a sample of patients with affective disorder presenting for treatment as part of the National Institute of Mental Health Collaborative Study of Depression and found that 24% of these patients reported serious problems with alcohol and 18% met diagnostic criteria for an alcohol use disorder. In an examination of patients with major depression, bipolar disorder, and controls participating in the National Institute of Mental Health Collaborative Program on the Psychobiology of Depression, Winokur and colleagues (1998) found that affective disorder patients had substantially higher rates of dual SUDs than did controls.

Dual diagnosis is also common among patients with anxiety disorders. In their review of studies of dual anxiety and SUDs, Kushner, Sher, and Beitman (1990) found that rates differ by type of anxiety disorder, with social phobia (ranging from 20% to 36% rate of dual diagnosis) and agoraphobia (ranging from 7.0% to 27.0% rate of dual

diagnosis) showing the highest rates of substance abuse comorbidity. Others have found a 22% rate of lifetime alcohol use disorder among patients with social phobia (Himle & Hill, 1991), a 10% to 20% rate for patients with agoraphobia (Bibb & Chambless, 1986), and up to a 12% rate of lifetime alcohol dependence among patients with obsessive-compulsive disorder (Eisen & Rasmussen, 1989). In addition, more attention is being given recently to dual substance abuse and PTSD in clinical samples. A growing literature examining this diagnostic combination finds high rates of dual diagnosis among patients with PTSD, with some findings as high as 80% (Keane, Gerardi, Lyons, & Wolfe, 1988). Research both with samples of veterans with PTSD and samples of women with assault- or trauma-related PTSD show strikingly high rates of comorbid substance abuse and dependence (see Stewart, Pihl, Conrod, & Dongier, 1998, for a review), as well as other disorders. Moreover, Breslau, Davis, Peterson, and Schultz (1997) interviewed a sample of 801 women and found that PTSD significantly increased the likelihood for later alcohol use disorder. Research with community mental health patients with several mental illnesses shows extremely high rates of co-occurring PTSD (14%–53%, usually undiagnosed; Grubaugh, Zinzow, Paul, Egede, & Frueh, 2011).

Research documents high rates of dual diagnosis among those with eating disorders. Higher rates of drug use have been found in samples of individuals with eating disorders than in controls (Krug et al., 2008), and studies of clinical samples show high overall rates of alcohol and drug use disorders. For example, Grilo, White, and Masheb (2009) assessed *DSM-IV* lifetime and current psychiatric disorder comorbidity in patients with binge-eating disorder and found that more than 73% of respondents had at least one lifetime diagnosis and 43% had at least one current psychiatric diagnosis, with almost 25% of the sample meeting criteria for a lifetime SUD. Several studies have shown variation in rates of SUDs across the different types of eating disorders—anorexia nervosa, bulimia nervosa, binge-eating disorder—and subsets of disorders within these (Root et al., 2010). In addition, rates of comorbidity, including that with SUDs, may be associated with eating disorder severity, with those with more severe symptoms of eating disorder showing the highest rates of comorbid SUDs (Spindler & Milos, 2007).

Some of the highest rates of comorbidity are found for patients with personality disorders, especially antisocial personality disorder (ASP). Studies show that comorbid ASP accelerates the development of alcoholism (Hesselbrock, Hesselbrock, & Workman-Daniels, 1986), and that 80% of patients with ASP have a history of problem use of alcohol (Schuckit, 1983). In a recent review of studies on dual SUDs and borderline personality disorder (BPD), Trull and colleagues (Trull, Sher, Minks-Brown, Durbin, & Burr, 2000) found that, across studies, more than 48% of patients with BPD met criteria for alcohol use disorders, and 38% of those with BPD met criteria for a drug use disorder. In a recent reanalysis of the NESARC data, Trull and colleagues (Trull, Jahng, Tomko, Wood, & Sher, 2010) found high rates of dual personality disorders and SUDs. More than one-quarter of those with ASP (26.65%) met criteria for drug dependence, although even higher rates of drug dependence were found for those with histrionic (29.72%) and dependent (27.34%) personality disorders.

Important work is now illustrating the need to think more broadly about dual and multiple comorbidities and how these span Axis I and Axis II disorders. For example,

a recent examination of data on generalized anxiety disorder from the NESARC study (Alegría et al., 2010) found a lifetime prevalence rate of generalized anxiety disorder with comorbid SUD of 2.04%. However, those with generalized anxiety disorder and comorbid SUD showed significantly higher rates of comorbidity of other psychiatric disorders than did those with generalized anxiety disorder alone, including higher lifetime rates of bipolar disorder, panic disorder, and ASP. A similar pattern was found for social anxiety in the NESARC data (Schneier et al., 2010): Respondents with both social anxiety disorder and comorbid alcohol use disorder were significantly more likely to earn diagnoses of mood, other anxiety, psychotic, and personality disorders, as well as additional SUDs and pathological gambling. Goldstein, Compton, and Grant (2010) examined rates of ASP in individuals with PTSD and how this combination of disorders affected risk of further comorbid psychiatric disorders. Compared to those with PTSD only, those with PTSD+ASP showed much higher rates of additional comorbid diagnoses. Specifically, those with PTSD+ASP met criteria for, on average, 5.7 additional lifetime Axis I diagnoses, whereas those with PTSD only met criteria for only 2.3 additional lifetime Axis I diagnoses. Rates of additional Axis II diagnosis were similar (2.5 additional Axis II diagnoses for those with PTSD+ASP versus 0.7 for those with PTSD only).

Wildes, Marcus, and Fagiolini (2008) examined rates of eating disorders in individuals with bipolar disorder and found that a subset of individuals with bipolar disorder and loss of control over eating showed elevated rates of substance use disorders. In another study of individuals with bipolar disorder, Bauer and colleagues (2005) interviewed inpatients using the Structured Clinical Interview for *DSM-IV* and found that rates of comorbidity with SUDs were high (33.8% current, 72.3% lifetime), but that almost 30% of respondents had comorbid bipolar, SUD, and anxiety disorders. Such findings illustrate the importance of expanding our thinking regarding dual diagnosis into multiple comorbidities.

As noted earlier, rates of tobacco dependence are high among individuals with mental health disorders. Studies indicate that more than 60% of adults with schizophrenia, 40% with bipolar disorder, and 30% with major depression in the United States smoke, compared to fewer than 20% in the overall adult population (Dickerson et al., 2012; Heffner, Strawn, DelBello, Strakowski, & Anthenelli, 2011). Similarly, research has found higher rates of smoking among those with a range of anxiety disorders, although directionality is unclear—there is evidence to suggest that smoking is a risk factor for panic disorder and generalized anxiety disorder (Moylan, Jacka, Pasco, & Berk, 2012).

Some speculate that those with mental health disorders who smoke may experience a more severe subtype of disorder than those who do not smoke. For example, Strong and colleagues (2010) examined differences in smoking behavior between those with no history of major depressive disorder, those with a single episode, or those with recurrent major episodes in 1,560 participants in the NCS-R. Those with comorbid recurrent major depression reported more smoking, greater nicotine dependence, more comorbid mental health disorders, and greater impairment in functioning than those with no or a single episode of major depression. Saiyad and El-Mallakh (2012) studied the impact of smoking on symptoms of bipolar disorders ($n = 134$) and found that those with bipolar disorder who smoked reported more severe symptoms of anxiety, depression, and mania. Others have suggested that smoking may be a marker

for a more chronic form of schizophrenia (Dalack & Meador-Woodruff, 1996) or a subtype of bulimia nervosa characterized by more depression and alcohol abuse (Sandager et al., 2008).

Dual Diagnosis in Patients With Primary Substance Use Disorders

Substance-abusing patients in treatment are a heterogeneous group, encompassing a range of substances and levels of severity. Nonetheless, researchers have found high rates of dual disorders across diverse samples of patients seeking substance abuse treatment (Arendt & Munk-Jorgensen, 2004; Falck, Wang, Siegal, & Carlson, 2004; Herz, Volicer, D'Angelo, & Gadish, 1990; Mirin, Weiss, Griffin, & Michael, 1991; Mirin, Weiss, & Michael, 1988; Penick et al., 1984; Powell, Penick, Othmer, Bingham, & Rice, 1982; Ross, Glaser, & Stiasny, 1988; Rounsaville, Weissman, Kleber, & Wilber, 1982; Watkins et al., 2004; Weissman & Myers, 1980). Findings of lifetime rates of psychiatric disorder range from 73.5% of a sample of cocaine abusers (Rounsaville et al., 1991) to 77% of a sample of hospitalized alcoholics (Hesselbrock, Meyer, & Keener, 1985) to 78% of a sample of patients in an alcohol and drug treatment facility (Ross, Glaser, & Germanson, 1988). Findings of current psychiatric disorder are similarly high, ranging from 55.7% of a group of cocaine abusers (Rounsaville et al., 1991) to 65% in a general substance-abusing sample (Ross, Glaser, & Germanson, 1988).

Further reflecting their diagnostic heterogeneity, substance abusers in treatment experience a range of comorbid psychiatric disorders. Among the most widely studied have been affective disorders, and treatment-seeking substance abusers show high rates of both major depression (Hasin, Grant, & Endicott, 1988; Hesselbrock et al., 1985; Merikangas & Gelernter, 1990; Mezzich et al., 1990; Miller, Klamen, Hoffmann, & Flaherty, 1996; Rounsaville, Weissman, Wilber, Crits-Christoph, & Kleber, 1982; Weissman & Myers, 1980) and bipolar disorder (Strakowski & DelBello, 2000). Miller and colleagues (1996) surveyed a sample of more than 6,000 substance abuse treatment patients from 41 sites and found that 44% had a lifetime history of major depression. In a review of comorbidity of affective and substance use disorders, Lynskey (1998) found that the prevalence of unipolar depression among patients receiving treatment for substance use disorders ranged from a low of 25.8% for lifetime depression in a sample of 93 alcohol-dependent men (Sellman & Joyce, 1996) to a high of 67% meeting a lifetime diagnosis of major depression among a sample of 120 inpatients (Grant, Hasin, & Harford, 1989). Busto, Romach, and Sellers (1996) evaluated rates of dual diagnosis in a sample of 30 patients admitted to a medical facility for benzodiazepine detoxification and found that 33% met *DSM-II-R* criteria for lifetime major depression.

Results from large studies of treatment-seeking substance abusers find that these patients show 5 to 8 times the risk of having a comorbid bipolar diagnosis (see Strakowski & DelBello, 2000, for a review). The importance of dual mental illness in substance-abusing samples lies in its link to functioning and treatment outcome. Burns, Teesson, and O'Neill (2005) studied the impact of dual anxiety disorders and/or depression on outcome of 71 patients seeking outpatient alcohol treatment. Comorbid patients showed greater problems at baseline (more disabled, drank more heavily) than did substance-abuse-only patients, a difference that persisted at a follow-up assessment 3 months later.

An extensive literature documents high rates of comorbid personality disorders in primary substance abusers (Khantzian & Treece, 1985; Nace, 1990; Nace, Davis, & Gaspari, 1991), especially ASP (Herz et al., 1990; Hesselbrock et al., 1985; Liskow, Powell, Nickel, & Penick, 1991; Morgenstern, Langenbucher, Labouvie, & Miller, 1997; Penick et al., 1984; Powell et al., 1982). In their evaluation of a large sample of treatment-seeking substance abusers, Mezzich and colleagues (1990) found that 18% of those with alcohol use disorders and almost 25% of those with drug use disorders met criteria for an Axis II disorder. Busto and colleagues (1996) found that 42% of their sample of patients undergoing benzodiazepine detoxification met *DSM-III-R* criteria for ASP. Morgenstern and colleagues (1997) assessed prevalence rates of personality disorders in a multisite sample of 366 substance abusers in treatment. Results showed that more than 57% of the sample met criteria for at least one personality disorder. ASP was the most prevalent (22.7% of the sample), followed by borderline (22.4%), paranoid (20.7%), and avoidant (18%) personality disorders. Moreover, the presence of a personality disorder doubled the likelihood of meeting criteria for a comorbid Axis I disorder. Brooner and colleagues (Brooner, King, Kidorf, Schmidt, & Bigelow, 1997) assessed psychiatric disorders in 716 opioid abusers on methadone maintenance therapy and found that 47% of the sample met criteria for at least one disorder, with ASP and major depression being the most common co-occurring diagnoses. In addition, psychiatric comorbidity was associated with more severe substance use disorder. Kokkevi, Stephanis, Anastasopoulou, & Kostogianni (1998) surveyed 226 treatment-seeking individuals with drug dependence in Greece and found a 59.5% prevalence rate of personality disorder, with more than 60% of these patients meeting criteria for more than one personality disorder. Furthermore, those with personality disorders were at twice the risk for meeting an additional Axis I diagnosis.

Findings are similar with anxiety disorders, with high rates of comorbid phobias (Bowen, Cipywnyk, D'Arcy, & Keegan, 1984; Hasin et al., 1988; Ross, Glazer, & Stiasny, 1988), panic disorder (Hasin et al., 1988; Penick et al., 1984), and obsessive-compulsive disorder (Eisen & Rasmussen, 1989) documented in substance-abusing populations. Thomas, Thevos, and Randall (1999) reported a 23% prevalence rate of social phobias in a large study of both inpatients and outpatients with alcohol dependence. Substance abusers also appear to be especially affected by PTSD (Cottler, Compton, Mager, Spitznagel, & Janca, 1992; Davis & Wood, 1999; Triffleman, Marmar, Delucchi, & Ronfeldt, 1995).

In an analysis of cocaine-dependent patients in the National Institute on Drug Abuse Collaborative Cocaine Treatment Study, Najavitis and colleagues (1998) found that 30.2% of women and 15.2% of men met *DSM-II-R* criteria for PTSD. Recently, Back and colleagues (2000) found that 42.9% of a sample of cocaine-dependent individuals met criteria for PTSD, and Bonin and colleagues (Bonin, Norton, Asmundson, Dicurzio, & Pidlubney, 2000) found a 37.4% rate of PTSD in a sample of patients attending a community substance abuse treatment program. In sum, the literature clearly documents high rates of dual substance abuse and psychiatric disorders for a variety of psychopathological conditions and in a range of patient populations. Findings from epidemiological studies show that dual diagnosis is relatively common in the general population, and results of clinical studies illustrate the frequency of dual diagnosis among individuals in treatment. That rates of dual diagnosis are similarly high in both mentally ill and in primary substance-abusing populations serves to

highlight the serious difficulties in having two separate and independent systems of care for mental illness and substance abuse (Grella, 1996; Ridgely, Lambert, Goodman, Chichester, & Ralph, 1998), because both populations of patients are quite likely to be suffering from both types of disorders.

CLINICAL IMPACT OF DUAL DISORDERS

The importance of dual diagnosis lies in its negative impact on the course and prognosis of both psychiatric and SUDs, as well as its influence on assessment, diagnosis, and treatment outcome. Individuals with dual disorders show more adverse social, health, economic, and psychiatric consequences than do those with only one disorder, and they show more severe difficulties, often a more chronic course of psychiatric disorder, and a poorer response to both mental health and substance abuse treatment. In the next section, we review the ways that dual diagnosis impacts three general areas: patient functioning, clinical care, and research.

IMPACT OF DUAL DIAGNOSIS ON FUNCTIONING

Dual diagnosis has a profound impact on many domains of functioning. This section reviews the many ways that dual diagnosis affects symptoms of mental illness, course of mental illness over time, cognitive functioning, and compliance with treatment.

Symptoms, Course of Illness, and Life Functioning Dual diagnosis severely impacts the severity and course of many disorders, especially among patients with serious mental illnesses such as schizophrenia, bipolar disorder, and recurrent major depression. Often these dually diagnosed individuals show a poorer and more chaotic course of disorder, with more severe symptoms (Alterman, Erdlen, Laporte, & Erdlen, 1982; Barbee et al., 1989; Hays & Aidroos, 1986; Negrete and Knapp, 1986), more frequent hospitalizations (Carpenter, Heinrichs, & Alphs, 1985; Drake & Wallach, 1989; Sonne, Brady, & Morton, 1994), and more frequent relapses than patients without co-occurring substance abuse (Linszen, Dingemans, & Lenior, 1994; O'Connell, Mayo, Flatow, Cuthbertson, & O'Brien, 1991; Sokolski et al., 1994). Haywood et al. (1995) found that substance abuse, along with medication noncompliance, was the most important predictor of more frequent rehospitalization among schizophrenia patients.

Recently, Margolese and colleagues (Margolese, Malchy, Negrete, Tempier, & Gill, 2004) compared three groups of schizophrenia patients: those with current SUD, those with lifetime but not current SUD, and those with no current or history of SUD. Patients with current SUD showed more positive symptoms than both other patient groups, had higher scores on measures of depression as compared to the single diagnosis group, and were more likely than the single diagnosis group to be noncompliant with their medications. Winokur and colleagues (1998) found that patients with drug abuse and bipolar disorder had an earlier age of onset of bipolar disorder than those with bipolar disorder alone, as well as a stronger family history of mania.

Nolen and colleagues (2004) rated patients with bipolar or schizoaffective disorder on severity of manic symptoms, severity of depressive symptoms, and number of illness episodes over a 1-year period ($n = 258$). Results showed that ratings for mania

severity were associated with comorbid substance abuse. Lehman, Myers, Thompson, and Corty (1993) compared individuals with dual mental illness and substance use diagnoses to those with just a primary mental illness and found that the dual diagnosis group had a higher rate of personality disorder and more legal problems. Hasin, Endicott, and Keller (1991) followed 135 individuals with dual mood and alcohol use disorders who were originally studied as part of the National Institute of Mental Health Collaborative Study on the Psychobiology of Depression. Although most had experienced at least one 6-month period of remission of the alcohol disorder at some point during the follow-up period, most had relapsed after 5 years. Mueller and colleagues (1994) examined the impact of alcohol dependence on the course of major depression over 10 years among individuals with depression who participated in the National Institute of Mental Health Collaborative Depression Study. Those who were alcohol dependent at baseline had a much lower rate of recovery from major depression than those with major depression alone, illustrating the negative impact of alcohol use disorders on the course of major depressive disorder.

Dual diagnosis is also a serious issue for patients with anxiety disorders such as PTSD (Najavitis, Weiss, & Shaw, 1997; Ouimette, Brown, & Najavitis, 1998). Overall, the combination of substance abuse and PTSD appears to be linked to higher rates of victimization, more severe PTSD symptoms in general, more severe subgroups of PTSD symptoms, and higher rates of Axis II comorbidity (Ouimette, Wolfe, & Chrestman, 1996). Saladin, Brady, Dansky, and Kilpatrick (1995) compared 28 women with both substance abuse and PTSD to 28 women with PTSD only and found that the dual diagnosis group reported more symptoms of avoidance and arousal, more sleep disturbance, and greater traumatic-event exposure than the PTSD-only group. Back and colleagues (2000) similarly found higher rates of exposure to traumatic events, more severe symptomatology, and higher rates of Axis I and Axis II disorders among cocaine-dependent individuals with PTSD as compared to those without lifetime PTSD. Moreover, evidence suggests that the combination of PTSD and cocaine dependence remains harmful over several years, with patients showing a greater likelihood of continued PTSD as well as revictimization several years after an initial substance abuse treatment episode (Dansky, Brady, & Saladin, 1998).

Dual diagnosis also exerts a profound impact on overall life functioning. Patients with severe mental illnesses such as schizophrenia who abuse substances appear to be particularly hard hit in this regard (see Bradizza & Stasiewicz, 1997, for a review; Kozaric-Kovacic, Folnegovic-Smalc, Folnegovic, & Marusic, 1995). Drake and colleagues consistently have found that individuals with schizophrenia and comorbid substance abuse show substantially poorer life adjustment than do individuals with schizophrenia without substance abuse, and eat fewer regular meals (Drake, Osher, & Wallach, 1989; Drake & Wallach, 1989). Havassy and Arns (1998) surveyed 160 frequently hospitalized adult psychiatric patients and found not only high rates of dual disorders (48% of patients had at least one current substance use disorder; of these, 55.1% met criteria for polysubstance dependence) but also that dual diagnosis was related to increased depressive symptoms, poor life functioning, lower life satisfaction, and a greater likelihood of being arrested or in jail. Research similarly shows that patients with dual affective and alcohol use disorders show greater difficulties in overall functioning and social functioning than do patients with depression (Hirschfeld, Hasin, Keller, Endicott, & Wunder, 1990) or bipolar disorder (Singh, Mattoo, Sharan, & Basu, 2005).

Newman, Moffitt, Caspi, & Silva (1998) examined the impact of different types of comorbidity (including but not limited to substance abuse–psychiatric disorder combinations) on life functioning in a large sample of young adults. Multiple-disordered cases showed poorer functioning than single-disordered cases in almost every area measured, including health status, suicide attempts, disruption in performance of daily activities, the number of months disabled because of psychiatric illness, greater life dissatisfaction, less social stability (more residence changes, greater use of welfare for support, greater rates of adult criminal conviction records), greater employment problems, lower levels of educational attainment, and greater reports of physical health problems. Weiss and colleagues (2005) examined the interplay between bipolar disorder and recovery from substance use disorders on a range of quality-of-life factors in a sample of 1,000 patients with current or lifetime bipolar disorder. Specifically, three groups were compared: those with no history of SUDs, those with past SUDs, and those with current SUDs. Results showed that the current-SUD group had the poorest functioning, and both SUD groups reported lower quality of life and higher lifetime rates of suicide attempts than did the non-SUD group. Moreover, the toxic effects of psychoactive substances in individuals with schizophrenia and bipolar disorder may be present even at use levels that may not be problematic in the general population (Lehman, Myers, Dixon, & Johnson, 1994; Mueser et al., 1990).

Cognitive Functioning Increasingly, clinicians and researchers are focusing on cognitive functioning in persons with dual disorders. There is a range of cognitive impairments associated with psychiatric disorders, particularly serious mental illness (e.g., schizophrenia, bipolar disorder). Individuals with schizophrenia spectrum disorders demonstrate cognitive impairments across a range of cognitive domains when compared to normative comparison samples (Heinrichs & Zakzanis, 1998). Although not as severe, individuals with affective disorders demonstrate similar impairments across a range of cognitive domains (Depp et al., 2007; Goldberg et al., 1993; Schretlen et al., 2007). These impairments are linked by modest to strong correlations to functional outcomes in schizophrenia (Green, 1996) and bipolar disorder (Dickerson et al., 2004; Dickerson, Sommerville, Origoni, Ringel, & Parente, 2001).

There is also evidence that, in samples of individuals with primary SUDs, chronic or sustained substance use can contribute to cognitive impairment and resulting brain dysfunction (Bowden, Crews, Bates, Fals-Stewart, & Ambrose, 2001; Rogers & Robbins, 2001). Moreover, cognitive impairment has been implicated in substance-abuse-treatment outcomes in this population (Aharonovich, Nunes, & Hasin, 2003; Fals-Stewart & Schafer, 1992). Such findings suggest that substance use may exacerbate existing cognitive impairment, which may, in part, contribute to the poorer outcomes experienced by persons with co-occurring serious mental illness (SMI) and SUD.

Although this recognition has prompted clinical research efforts to adapt and develop new substance abuse interventions designed to accommodate some of the cognitive and motivational impairments associated with SMI (e.g., Addington, el-Guebaly, Campbell, Hodgins, & Addington, 1998; Bellack, Bennett, Gearon, Brown, & Yang, 2006; Ziedonis & George, 1997), other research efforts have been directed toward further description and explication of the role of cognitive

impairment in individuals with dual diagnosis. The majority of this work has focused on SMI samples. On the one hand, there is concern about the possible exacerbation of existing cognitive impairment resulting from substance use among individuals with dual disorders, suggesting that these individuals would demonstrate poorer cognitive functioning when compared to those without SUD. On the other hand, some data suggest that engaging in behaviors necessary to obtain access to substances requires a higher level of functioning (Dixon, 1999; Mueser et al., 1990), and, thus, these individuals with dual disorders would have better cognitive functioning than individuals without SUD.

With regard to cognitive functioning, the data are in fact mixed and overall suggest that there are few differences between those with SMI who have a current or history of SUD and those who do not. In a meta-analysis of 22 studies investigating neurocognitive functioning among individuals with schizophrenia, Potvin, Joyal, Pelletier, and Stip (2008) found that there was no difference on a composite score of cognitive functioning between those with SUD and those without. Furthermore, they found few differences between groups on specific cognitive domains or specific cognitive measures. Depp et al. (2007) also found no differences in cognitive functioning among a sample of individuals with bipolar disorder with and without SUDs. In contrast, Carey, Carey, and Simons (2003), in a sample of individuals with schizophrenia spectrum and bipolar disorders, found that those with a current SUD or former SUD both demonstrated better cognitive functioning than those who had never used substances.

The interpretation of these data is complicated by several substantive and methodological issues. First, there is some indication that impairment may vary depending on primary substance of abuse. Across the meta-analytic data, alcohol use was associated with poorer working memory performance, whereas cannabis use was associated with better problem solving and visual memory performance (Potvin et al., 2008). This finding is consistent with neuropsychological data from SUD samples without psychiatric diagnoses, where alcohol is associated with greater impairments than other drugs such as cocaine (Goldstein et al., 2004). However, types of substances are not always accounted for in dual disorder studies (e.g., Carey et al., 2003). Second, consistent with methodological limitations across the dual diagnosis research literature, the rigor with which samples have been characterized has been quite variable. Some studies have relied on chart diagnoses as opposed to diagnostic interview to identify SUD, few have verified drug status with urinalysis, and others have failed to characterize the severity, recency, or chronicity of substance use. With regard to the latter, analyses included in the Potvin et al. (2008) study indicated that as age increased, so did the cognitive impairment among those with SUD, suggesting that chronicity of use may be a moderating factor in cognitive functioning among dual disorders. Similarly, Carpenter and Hittner (1997) found that lifetime use of alcohol or cocaine (i.e., number of years of regular use) were the strongest predictors of cognitive impairment among a sample of individuals with mixed psychiatric diagnoses (affective and anxiety disorders) and SUDs.

These latter findings raise the related question of how cognitive impairment changes over time as a result of substance use in individuals with dual disorders. Few investigations have addressed this question. Using a group comparison design with carefully characterized samples, Carey et al. (2003) found no difference in

cognitive functioning between individuals with SMI and current SUD versus those with past history of SUD (defined as not meeting full criteria for the past 6 months). Peer, Bennett, and Bellack (2009) compared individuals with schizophrenia who met *DSM-IV* criteria for current cocaine dependence and those who met criteria for remission on a brief neuropsychological battery and found few differences. This study also included a parallel analysis of samples of individuals with affective disorders and cocaine dependence versus remission, which yielded similar results. Although these studies used rigorous diagnostic criteria to characterize the samples, they are limited by their cross-sectional nature. That is, they did not evaluate change within subjects in cognitive functioning as a result of discontinuation of substance use.

At least two longitudinal studies have been conducted that address this question. A brief longitudinal study of inpatients with schizophrenia with or without current cocaine dependence at admission found few changes in cognition as a result of abstinence from cocaine over an 18-day study period (Cooper et al., 1999). Furthermore, there were few differences in cognition between groups at baseline or at follow-up. McCleery, Addington, and Addington (2006) followed 183 individuals with a first episode of psychosis over a 2-year study period and assessed cognition and substance use. Results indicated that cognition largely remained stable over time, while substance use declined over the study period. Together these findings suggest that cognitive functioning may be relatively static among individuals with dual disorders. Indeed, in the general SUD literature, longitudinal data suggest there are only slight and/or inconsistent improvements in neurocognitive functioning after a period of abstinence from substances (Bates, Voelbel, Buckman, Labouvie, & Barry, 2005; Di Sclafani, Tolou-Shams, Price, & Fein, 2002; Horner, 1999).

There are at least two possible interpretations of these data: (1) given the significant cognitive impairment associated with SMI, substance use causes only minimal additional impairment; and (2) the toxic effects of substance use on cognition are not easily resolved following abstinence. In part, this research may be limited by the lack of sensitivity of the neuropsychological measures used for these particular research questions. With further advances in cognitive neuroscience, more refined measures that are more tightly linked to brain structures and functions impacted by chronic substance use will likely be developed (Rogers & Robbins, 2001). Although candidate brain structures and neurotransmitter pathways are increasingly being identified in the general SUD literature (e.g., Goldstein et al., 2004; Goldstein & Volkow, 2002), significantly more work is needed to understand the specifics of cognitive functioning in dual disorders, both with regard to preexisting impairment as well as a sequelae of chronic substance use.

Treatment Noncompliance and Violence Substance abuse often interferes with compliance with both behavioral and psychopharmacological treatments. Lambert, Griffith, and Hendrickse (1996) surveyed patients on a general psychiatry unit in a Veterans Administration medical center and found that discharges against medical advice (AMA) were more likely to occur among patients with alcohol and/or substance use disorders. Pages and colleagues (1998) similarly assessed predictors of AMA discharge in psychiatric patients. The presence of SUD and a greater quantity and frequency of substance use were among the most important predictors. Owen and colleagues (Owen, Fischer, Booth, & Cuffel, 1996) followed a sample of 135 inpatients

after discharge and found that medication noncompliance was related to substance abuse, and that this combination was significantly associated with lack of outpatient contact in the follow-up period. Specifically, those with dual diagnoses were more than 8 times more likely to be noncompliant with their medication. In a large-scale study of factors related to medication adherence in schizophrenia patients, Gilmer and colleagues (2004) found that substance abusers were less likely to be adherent to antipsychotic medication regimens than were schizophrenia patients who did not abuse substances.

Similar results were found in a review of factors that impede use of medication in individuals with bipolar disorder (Velligan et al., 2009): Many studies have found that substance use is a critical barrier to medication adherence. Such findings are especially important when linked to functioning and service use. For example, schizophrenia patients who were nonadherent with their medications were more than 2.5 times more likely to be hospitalized than those who were adherent (Gilmer et al., 2004). Verduin, Carter, Brady, Myrick, and Timmerman (2005) compared bipolar only, alcohol-dependent only, and comorbid bipolar and alcohol-dependent patients on several treatment variables, including number of outpatient psychiatric visits and length of psychiatric hospitalizations, in the year leading up to and including an index hospitalization at a veterans' hospital from 1999 through 2003. The comorbid group had fewer outpatient psychiatric visits and shorter inpatient hospitalizations than did either of the single disorder groups.

For many disorders, substance abuse and its associated noncompliance with treatment is linked not only to poorer outcomes but also to greater risk for violence (Marzuk, 1996; Poldrugo, 1998; Sandberg, McNiel, & Binder, 1998; Scott et al., 1998; Soyka, 2000; Steadman et al., 1998; Swanson, Borum, Swartz, & Hiday, 1999; Swartz et al., 1998) and suicide (Cohen, Test, & Brown, 1990; Goodwin & Jamison, 1990; Karmali et al., 2000; Landmark, Cernovsky, & Merskey, 1987; Pages, Russo, Roy-Byrne, Ries, & Cowley, 1997; Verduin et al., 2005). In terms of violence, Fulwiler, Grossman, Forbes, and Ruthazer (1997) compared differences between two groups of outpatients with chronic mental illness: those with and without a history of violence. The only significant differences between the two groups involved alcohol or drug use. McFall and colleagues (McFall, Fontana, Rasking, & Rosenheck, 1999) examined 228 male Vietnam veterans seeking inpatient treatment for PTSD and found that levels of substance abuse were positively correlated with violence and aggression. The combination of schizophrenia and ASP appears to put people at high risk for violence, especially when they are drinking (Joyal, Putkonen, Paavola, & Tiihonen, 2004).

In their recent examination of population-based registers of hospital discharge diagnoses and violent crime in a Swedish sample over 30 years, Fazel, Lichtenstein, Grann, Goodwin, and Langstrom (2010) found that risk for violent crime among individuals with bipolar disorders was almost entirely due to substance abuse comorbidity, with those with bipolar-only diagnoses showing extremely low risk for violent crime. Such findings illustrate the problematic impact of substance use on violence in individuals with psychiatric disorders.

Research also shows links between dual disorders and rate of suicide. In an analysis of epidemiological data from the NESARC, Oquendo and colleagues found that lifetime rates of suicide attempts were higher for those with dual bipolar disorder and alcohol use disorders (25.29%) than for respondents with bipolar disorder alone

(14.78%) (Oquendo et al., 2010). Pages and colleagues (1997) surveyed 891 psychiatric inpatients with major depressive disorder and found that both substance use and substance dependence were associated with higher levels of suicidal ideation. Potash and colleagues (2000) examined the relationship between alcohol use disorders and suicidality in bipolar patients and found that 38% of subjects with dual bipolar and alcohol use disorders had attempted suicide, as compared to 22% of those with bipolar disorder only. Recently, McCloud, Barnaby, Omu, Drummond, and Aboud (2004) examined alcohol disorders and suicidality (defined as any record of self-harm or thoughts or plans of self-harm or suicide written in the medical record) in consecutive admissions to a psychiatric hospital. Problem drinking (as measured by the Alcohol Use Disorders Identification Test [AUDIT]) was strongly related to suicidality, with higher AUDIT scores (representing greater severity of problems with alcohol) showing higher rates of suicidality.

Importantly, those with multiple comorbidities—patients who have more than two comorbid diagnoses—are at even higher risk for suicide. In such cases, the added impact on suicidality of trauma in general or comorbid PTSD in particular is great. Tarrier and Picken (2010) examined rates of suicide in individuals with dual schizophrenia and substance use disorders and found that rates of suicidality (based on scores on the Beck Suicidality Scale) were higher among those with comorbid PTSD. Cacciola and colleagues (Cacciola, Koppenhaver, Alterman, & McKay, 2009) identified four groups among a sample of 466 male veterans: (1) substance use disorder only; (2) substance use disorder + PTSD; (3) substance use disorder + PTSD + another Axis I disorder; and (4) substance use disorder + another Axis I disorder. Lifetime rates of both suicidal ideation and suicide attempts were highest in the substance use disorder + PTSD + another Axis I disorder group. Such findings illustrate the ways that multiple comorbidities can further increase risk for suicidality.

Impact of Dual Diagnosis on Clinical Care and Related Factors

Dual diagnosis impacts clinical care on many levels. This section reviews the many ways that dual diagnosis impacts service use and health-care costs, as well as related factors such as medical illness, legal problems, and homelessness.

Service Utilization and Health Care Costs The fact that clinical settings routinely demonstrate higher rates of dual diagnosis patients points to the fact that having both psychiatric and SUDs increases rates of seeking treatment. Increased service utilization among the dually diagnosed has been borne out in both large-scale household surveys and clinical studies. For example, Helzer and Pryzbeck (1988) examined data from the ECA study and found that, for respondents of both sexes with alcohol use disorders, the number of additional non-substance-use-disorder diagnoses had a significant impact on seeking treatment: Those with more diagnoses reported greater utilization of treatment services. Grant (1997) examined the influence of comorbid major depression and substance abuse on rates of seeking alcohol and drug treatment in data collected from the National Longitudinal Alcohol Epidemiological Survey (NLAES; Grant et al., 1994). The percentage of individuals with alcohol use disorders seeking treatment practically doubled, from 7.8% to 16.9%, when a comorbid major depressive disorder was also present. Interestingly, the greatest rate

of seeking treatment (35.3%) was found among respondents who met criteria for all three disorders—alcohol, drug, and depression—illustrating how the term *dual diagnosis* is somewhat misleading, because some individuals have two or more substance use and psychiatric disorders, and each might have an additive effect on negative outcomes.

Similarly, Wu, Kouzis, and Leaf (1999), analyzing data from the NCS, found that although 14.5% of patients with a pure alcohol disorder reported using mental health and substance abuse intervention services, more than 32% of patients with comorbid alcohol and mental disorders used such services. Menezes and colleagues (1996) studied the impact of substance use problems on service utilization over 1 year in a sample of 171 individuals with serious mental illness. Although the number of inpatient admissions was equivalent for those with dual disorders and those with mental illness only, the dual diagnosis group used psychiatric emergency services 1.3 times more frequently and spent 1.8 times as many days in the hospital as did the single disorder group.

Given their increased rates of service utilization, it is not surprising that dual diagnosis patients generally accrue greater health care costs than do patients with a single diagnosis (Maynard & Cox, 1998; McCrone et al., 2000). Dickey and Azeni (1996) examined the costs of psychiatric treatment for more than 16,000 seriously mentally ill individuals with and without comorbid SUDs. Patients with dual diagnoses had psychiatric treatment costs that were nearly 60% higher than the costs of psychiatrically impaired individuals without substance abuse. Interestingly, most of the increased cost was owing to greater rates of inpatient psychiatric treatment, suggesting that the impact of substance abuse on psychiatric symptoms and illness relapse is realized when patients require costly psychiatric hospitalization. Garnick, Hendricks, Comstock, and Horgan (1997) examined health insurance data files over 3 years from almost 40,000 employees and found that those with dual diagnoses routinely accrued substantially higher health care costs than those with substance abuse only. Such findings suggest that individuals with dual disorders access the most expensive treatment options (inpatient hospitalization, visits to emergency rooms) that are short-term in order to manage acute distress and fail to get the comprehensive and ongoing care they require.

These findings on rates of services use can be perplexing. For example, if dual diagnosis patients are accessing more and more expensive services, why do they consistently have more severe psychiatric symptoms, more substance-related problems, and poorer outcomes than do those with single disorders? As noted earlier, dual diagnosis patients appear to access expensive but short-term or acute treatment options more often while being noncompliant or not adhering to longer-term medication and outpatient treatment regimens. Other factors include lack of integrated care, as well as problems associated with treating more than one disorder (Watkins, Burnam, Kung, & Paddock, 2001). In addition, researchers recently have begun to more closely examine the quality of services accessed by dual diagnosis patients. For example, in their study of patients with bipolar disorder with and without comorbid substance use disorders, Verduin and colleagues (2005) found that patients with bipolar disorder and comorbid substance abuse were less likely than patients with substance abuse alone to be referred to intensive substance abuse treatment.

Watkins and colleagues (2001) looked at the delivery of appropriate care to probable dual-diagnosis patients assessed as part of the Healthcare for Communities Survey (a study of a subset of respondents from the Community Tracking Study, a nationally representative study of the civilian, noninstitutionalized people in the United States [see Kemper et al., 1996, for details]). Appropriate care included medications for severe mental illness (a mood stabilizer for bipolar disorder, antipsychotic medication for a psychiatric disorder), medications and/or psychosocial interventions for anxiety disorders or major depression, and at least four sessions of any sort of treatment in the past year. In addition, variables addressed included whether patients are receiving integrated care for dual disorders (receiving both mental health and substance abuse treatment from one provider) or comprehensive substance abuse treatment (defined as including inpatient or outpatient substance use treatment that included a physical examination, a mental health evaluation, or job or relationship counseling). Results showed that 72% of dual-diagnosis patients did not receive any specialty mental health or substance abuse services (i.e., services provided by a mental health or substance abuse professional rather than a primary care physician), 8% received both mental health and substance abuse treatment (either integrated or by different providers), 23% received appropriate mental health care, and 9% received comprehensive substance abuse treatment.

Other studies have found a disconnect between services accessed and services needed in dual diagnosis samples (Najavits, Sullivan, Schmitz, Weiss, & Lee, 2004). Such findings suggest that the complicated clinical picture presented by dual diagnosis patients makes it difficult for patients and providers to determine and administer appropriate care.

Physical Illness Dual diagnosis puts people at risk for different forms of illness and disease. This is especially true in the case of dual mental health disorders and tobacco dependence. The negative health effects of smoking are well known, and those with mental health disorders who smoke similarly share these risks. However, some populations fare even worse when it comes to the negative effects of smoking. For example, people with serious mental illness (SMI) represent a special population that is even more markedly affected by the negative effects of smoking than other groups of smokers. People with SMI are known to suffer from a range of life threatening medical conditions at rates that are significantly higher than those in the general population (Jeste, Gladsjo, Lindamer, & Lacro, 1996; Muir-Cochrane, 2006) and are also more likely to have multiple chronic illnesses (Carney & Jones, 2006; Carney, Jones, & Woolson, 2006; Dickerson et al., 2006). This high rate of medical comorbidity results in worsened psychosis and psychiatric symptoms, lowered quality of life, and higher rates of mortality in people with SMI (Auquier, Lancon, Rouillon, Lader, & Holmes, 2006; Dixon, Postrado, Delahanty, Fischer, & Lehman, 1999; Dixon et al., 2007).

Smoking and tobacco dependence significantly impacts, complicates, or is known to be a primary cause of, the medical diseases that lead to significantly elevated rates of mortality for people with SMI (Compton, Daumit, & Druss, 2006). In addition to the devastating health effects, smoking and tobacco dependence confer other negative consequences for those with SMI. Smoking increases the metabolism of some antipsychotic medications, producing reduced antipsychotic blood levels and requiring substantial increases in medication dosages in some cases (Goff, Henderson, & Amico,

1992; Ziedonis, Kosten, Glazer, & Frances, 1994). SMI smokers have been found to show a poorer course of illness, with earlier onset and more psychiatric hospitalizations (Goff et al., 1992; Sandyk & Kay, 1991; Ziedonis et al., 1994). Finally, other important consequences of smoking for people with SMI include the high financial cost of smoking in people with limited income (Steinberg, Williams, & Ziedonis, 2004), as well as additional negative social perceptions in a population that is already subject to significant social stigma.

One of the most significant health problems among those with dual diagnosis is greatly increased risk for HIV and AIDS. People with schizophrenia and other severe mental illness are now one of the highest-risk groups for HIV (Gottesman & Groome, 1997; Krakow, Galanter, Dermatis, & Westreich, 1998), and data indicate that substance use substantially increases the likelihood of unsafe sex practices (Carey, Carey, & Kalichman, 1997) and other high-risk behaviors in those with mental illness. For example, McKinnon and colleagues (McKinnon, Cournos, Sugden, Guido, & Herman, 1996) found that 17.5% of a sample of psychiatric patients had a history of injection drug use, 35% reported using drugs during sex, and 30% traded sex for drugs—all substance use behaviors that are highly risky in terms of the transmission of HIV and AIDS. In their sample of 145 psychiatric inpatients and outpatients in Australia, Thompson and colleagues (1997) found that 15.9% of dual diagnosis patients reported injection drug use, a figure that is 10 times higher than that found in the general population. Hoff, Beam-Goulet, and Rosenheck (1997) examined data from the 1992 National Survey of Veterans and found that the combination of PTSD and substance abuse increased the risk of HIV infection by almost 12 times over individuals with either disorder alone.

There is increasing evidence that other physical illnesses and high-risk health habits are also found more often in people with dual disorders. Stuyt (2004) found that 29.7% of a dual diagnosis sample had hepatitis C, a rate that is 16 times higher than that found in the general population. Salloum, Douaihy, Ndimbie, and Kirisci (2004) examined physical health and disorders in three groups of psychiatric patients hospitalized on a dual diagnosis treatment unit: a group with both alcohol and cocaine dependence, a group with alcohol dependence only, and a group with cocaine dependence only. Results showed that the group with both alcohol and cocaine dependence showed higher rates of a range of medical problems, including multiple hepatitis infections, than both single diagnosis groups.

Jones and colleagues (2004) examined physical health problems among people with severe mental illness and found that 74% of the sample was treated for one chronic health condition, and 50% was treated for two or more. The two most highly prevalent chronic health conditions—pulmonary disease and infectious disease—were both associated with substance use disorders in this sample. Moreover, results of regression analysis showed that substance abuse, along with age and obesity, was a significant predictor of health problem severity. Ouimette, Goodwin, and Brown (2007) identified medical problems in SUD patients with and without PTSD. Those with dual SUD + PTSD had more cardiovascular, neurological, and total physical symptoms than those with SUDs alone. Others have found high rates of mortality and other dangerous health conditions among those with dual diagnosis (Batki et al., 2009; Dickey, Dembling, Azeni, & Normand, 2004; Lambert, LePage, & Schmitt, 2003). Importantly, these higher rates of physical health problems can

serve as additional barriers to achieving important recovery goals (Conover, Arno, Weaver, Ang, & Ettner, 2006).

Legal Problems There is also evidence that individuals with dual diagnoses have more frequent contacts with the legal system. Clark, Ricketts, and McHugo (1999) followed a sample of individuals with mental illness and substance use disorders over 3 years to longitudinally examine legal involvement and its correlates in this population. The sample consisted of 203 patients receiving treatment in a dual diagnosis treatment program. Cost and use data were collected from a range of sources, including police, defenders, prosecutors, and jails. Interestingly, while rates of arrest were certainly high, patients were 4 times more likely to have encounters with the legal system that did not result in arrest. This suggests that frequency of arrest, although significant, is an underrepresentation of the frequency of contact that dual diagnosis patients have with the legal system. In addition, continued substance abuse over the follow-up period was significantly associated with a greater likelihood of arrest. Among samples of incarcerated prisoners, rates of severe mental illnesses and co-occurring psychiatric disorders are far higher than in the general U.S. population (Wolff et al., 2011).

Homelessness The combination of mental illness and substance abuse also increases risk for homelessness. In a study of patients with schizophrenia, Dixon (1999) found that those who used substances experienced not only greater psychotic symptoms and relapses, a higher incidence of violent behavior and suicide, elevated rates of HIV infection, increased mortality, and higher rates of treatment and medication non-compliance, but they were also more likely to live in an unstable housing situation or be homeless. Caton and colleagues (1994) compared a sample of mentally ill homeless men to a sample of mentally ill men who were not homeless and found higher rates of drug use disorders among the homeless group. Leal, Galanter, Dermatis, and Westreich (1999) assessed homelessness in a sample of 147 patients with dual diagnosis and found that those in the group with so-called protracted homelessness (no residence for 1 year or more) were significantly more likely than those patients without protracted homelessness to report a history of injection drug use. Recently, Folsom et al. (2005) examined risk factors for homelessness and patterns of service use among those who are homeless in a large sample ($n = 10{,}340$) of patients with severe mental illness from a large public mental health system in southern California. Homelessness was associated with a range of variables, including substance abuse—60.5% of the homeless mentally ill group showed a substance use disorder as compared to 20.9% of the non-homeless mentally ill group. Moreover, results of multivariate logistic regression showed that those with mental illness and substance abuse were more than 4 times as likely to be homeless as were patients who did not abuse substances.

Issues for Women With Serious Mental Illness and Substance Abuse Importantly, dual diagnosis is often particularly problematic for individuals who are also otherwise underserved. As noted, individuals with schizophrenia appear to be particularly hard hit by the additional difficulties of SUD. Another such population is women with severe mental illness and substance abuse. Research on women with dual diagnoses has shown that those with comorbid severe mental illness and substance abuse show

poorer retention in treatment (Brown, Melchior, & Huba, 1999) and elevated levels of anxiety, depression, and medical illness (Brunette & Drake, 1998), as well as being more difficult to engage in treatment and more under-represented in treatment overall (Comtois & Ries, 1995). In addition, women with dual diagnoses appear to have alarming rates of sexual and physical victimization that are substantially higher than those observed among women in the general population (Gearon & Bellack, 1999; Goodman, Rosenburg, Mueser, & Drake, 1997). Prevalence rates for physical victimization for women with serious mental illness range between 42% and 64% (Jacobson, 1989), and other research finds that 21% to 38% of women with serious mental illness report adult sexual abuse (Goodman, Dutton, & Harris, 1995). Among women receiving treatment in a residential therapeutic community, 49% reported physical abuse and 40% reported sexual abuse (Palacios, Urmann, Newel, & Hamilton, 1999). Data from 28 women and 24 men with serious mental illness and SUDs indicated that, when compared with men, women were more likely to report being physically (60% of women vs. 29% of men) and sexually (47% of women vs. 17% of men) victimized (Gearon, Bellack, Nidecker, & Bennett, 2003).

In addition, issues related to pregnancy and parenting often affect women with dual diagnosis. Grella (1997) summarized some of the many difficulties in terms of providing services for pregnant women with dual disorders, including receiving adequate prenatal care, use of substances and psychiatric medications while pregnant, and lack of coordinated treatment planning and provision among medical, psychiatric, and addictions professionals. Kelly and colleagues (1999) examined the medical records of all women delivering babies in California hospitals in 1994 and 1995 and found that women with both psychiatric and substance use diagnoses were at greatly elevated risk of receiving inadequate prenatal care. There are also substantial barriers to treatment and medical care for these women, including fears of losing custody of the unborn child or their other children, lack of medical insurance, and the often disjointed nature of available services for the medical and psychiatric care of these patients (Grella, 1997). Finally, when compared to men, women with dual diagnosis may have different treatment needs. Grella (2003) compared differences in substance use and treatment histories and perceptions of service needs between men and women diagnosed with severe mental illness (mood or psychotic disorders) on admission to inpatient drug treatment. Women reported greater needs for family and trauma-related services, and women with psychotic disorders had the greatest level of need of all the groups for basic services.

Provision of Treatment and Treatment Outcome

Co-occurring SUDs raise problems for interventions that have been designed to impact specific psychiatric symptoms, or ones that have been validated on samples that have excluded dual diagnosis patients. In addition, clinicians often experience difficulties in making referrals for dual diagnosis patients in the current system of single disorder treatment that effectively separates the treatment systems for mental illness and substance abuse. The fact that patients must often be forced into single diagnostic categories no doubt results in SUDs being overlooked or ignored by treatment professionals who have expertise in treating only single conditions or in dual diagnosis patients not receiving both the psychiatric and the substance abuse

treatment they require (Blanchard, 2000). Patients with dual diagnosis are more difficult to treat and show poorer retention in treatment as well as poorer treatment outcomes as compared to single disorder patients. Such findings tend to be true both for patients with primary mental illness and co-occurring substance abuse (see Drake, Mercer-McFadden, Mueser, McHugo, & Bond, 1998, and Polcin, 1992 for reviews; Goldberg, Garno, Leon, Kocsis, & Portera, 1999), as well as for patients identified through substance abuse treatment programs with comorbid mental illness (Glenn & Parsons, 1991; Ouimette, Ahrens, Moos, & Finney, 1998; Rounsaville, Kosten, Weissman, & Kleber, 1986). An early study by McLellan, Luborsky, Woody, O'Brien, and Cruley (1983) found that higher psychiatric severity was associated with poorer treatment outcome among alcohol and drug abuse treatment patients. Tomasson and Vaglum (1997) examined the impact of psychiatric comorbidity on 351 treatment-seeking substance abusers over a 28-month period and found that patients with comorbid psychiatric disorders at admission showed worse outcome in terms of mental health functioning at follow-up.

Ouimette, Gima, Moos, and Finney (1999) reported findings of a 1-year follow-up of three groups of patients with dual substance use and psychiatric disorders (psychotic disorders, affective/anxiety disorders, and personality disorders) as compared to a group of substance abuse–only patients. Although all the groups showed comparable decreases in substance use at follow-up, patients with dual diagnoses showed greater levels of psychological distress and psychiatric symptoms and lower rates of employment than did patients with only SUDs. In a 3-year follow-up of a sample of patients with alcohol use disorders, Kranzler, Del Boca, and Rounsaville (1996) found that the presence of comorbid psychiatric disorders, including depression and ASP, is generally associated with worse 3-year outcomes.

Thomas, Melchert, and Banken (1999) examined treatment outcome in 252 patients in substance abuse treatment and found the likelihood of relapse within the year following treatment was significantly increased in patients with dual personality disorders. Specifically, 6% of patients with personality disorders were abstinent 1-year posttreatment, as compared with 44% of those with no diagnosed personality disorders. A study by Havassy, Shopshire, and Quigley (2000) examined the effects of substance dependence on treatment outcome in 268 psychiatric patients following two different case management programs. Regardless of program, dual diagnosis patients showed more negative outcomes than patients with only a psychiatric disorder.

Such results illustrate that the dually diagnosed fare worse than patients with either SUDs or psychiatric disorders alone following treatment. Importantly, the fact that dual-diagnosis patients are often found to still be adversely affected by psychiatric symptomatology following substance abuse treatment is a stark reminder that treatment strategies have yet to evolve that effectively address symptoms of both types of disorders.

IMPACT OF DUAL DISORDERS ON ASSESSMENT AND DIAGNOSIS

There are numerous ways that dual diagnosis affects assessment and diagnosis, including symptom overlap, multiple impairments owing to different disorders, and substance-induced disorders resembling psychiatric disorders.

Symptom Overlap

Symptom overlap is a significant complication in terms of assessment and diagnosis. The symptoms of many psychiatric disorders overlap with those of substance use disorders, making diagnosis of either class of disorders difficult. For example, *DSM* lists problems in social functioning as symptoms of both schizophrenia and SUDs. That some criteria can count toward multiple diagnoses can potentially increase comorbidity rates and can make diagnosis of substance abuse difficult. This overlap can work against identification of the psychiatric disorder in some cases. For example, high rates of dual substance use and bipolar disorders lead to an underdiagnosis of bipolar disorder, because of the often incorrect assumption that the behavioral manifestations of bipolar disorder are secondary to substance use (Evans, 2000). Others (Brady, Killeen, Brewerton, & Lucerini, 2000; Brunello et al., 2001) suggest that underdiagnosis can also be an issue with dual PTSD and substance use disorders.

Multiple Impairments Owing to Different Disorders

Substance use disorders are often overlooked in mental health settings in which patients present with a range of acute impairments that exert a negative impact on overall functioning. There is often diagnostic confusion in terms of whether a given impairment results from substance abuse, psychiatric disorder, both, or neither. For example, it is exceedingly difficult to determine the impact of substance abuse when serious mental illness profoundly affects all areas of functioning. Patients with severe mental illness in particular have a range of impairments in social, cognitive, occupational, and psychological functioning, and evaluating the negative impact of substance abuse is difficult when the functioning of individuals in this patient population is so poor to begin with. Moreover, *DSM-IV* diagnoses of substance abuse and dependence are based for the most part on diagnostic criteria that reflect substance use becoming more pervasive in a person's life and interfering with normal functioning. For example, criteria involve substance use impairing one's ability to work, engage in relationships, complete responsibilities, and participate in activities. However, such factors often do not apply to many patients with mental illness whose substantial level of impairment associated with the psychiatric disorder often precludes them from having a job, being in relationships, or engaging in other activities. It becomes unclear how to measure the negative impact of substance use when there are few competing demands, activities, or responsibilities to be disrupted.

Substance-Induced Disorders Resemble Psychiatric Disorders

Diagnosis of psychopathology in the presence of substance abuse and dependence is especially difficult because symptoms of substance use and withdrawal can resemble psychiatric disorders (Schuckit, 1983; Schuckit & Monteiro, 1988). Schuckit and Monteiro (1988) review several instances in which symptoms of substance abuse resemble or mimic psychiatric symptoms. For example, long-term alcohol use and withdrawal can lead to psychotic symptoms, and abuse of amphetamines often results in psychotic symptoms that are identical to schizophrenia. Alcohol abuse and withdrawal also resemble symptoms of anxiety disorders (Kushner, Sher, & Beitman,

1990). Panic and obsessive behavior are often found with stimulant use and withdrawal from depressant drugs (Schuckit, 1983). Because symptoms of substance use and withdrawal can resemble psychiatric symptoms, differential diagnosis may be confounded. The lack of clear rules for differential diagnosis has important implications. Rates of dual diagnosis might be inflated, with individuals experiencing psychiatric disorders concurrent with alcohol or drug dependence being counted among those with dual disorder, although many of these symptoms will likely fade following a period of abstinence.

Incorrect treatment decisions may be made if interventions are aimed at what appear to be acute symptoms of psychiatric disorder but are, in fact, substance-induced symptoms. For example, Rosenthal and Miner (1997) review the issue of differential diagnosis of substance-induced psychosis and schizophrenia and stress that medicating what appears to be acute psychosis due to schizophrenia but is actually substance-induced psychosis is not only incorrect but also ineffective treatment. Schuckit and colleagues (1997) suggest that too little attention has been paid to the "independent versus concurrent distinction" as it applies to dual diagnosis. Some alcoholics suffer from long-term psychiatric disorders that are present before, during, and after alcohol dependence and require treatment independent of that for their alcohol abuse or dependence.

On the other hand, many individuals present with substance-induced disorders, including depression, anxiety, and psychosis, that will remit after several weeks of abstinence. They suggest that much dual diagnosis, while distressing and clinically relevant in the short-term, is temporary, likely to improve after several weeks, and thus holds different clinical and treatment implications from a true, independent psychiatric disorder. Their data, taken from the Collaborative Study on the Genetics of Alcoholism, shows that the majority of alcohol-dependent men and women did not meet diagnostic criteria for an "independent" mood or anxiety disorder that occurred outside of the context of the alcohol dependence. Specifically, there was no increased risk of a range of disorders in the alcohol-dependent sample, including major depression, obsessive-compulsive disorder, or agoraphobia. In contrast, there was an increased risk of independent bipolar, panic disorder, and social phobia.

Others have also found that a majority of dual diagnosis patients have concurrent psychiatric diagnoses that are likely owing to the effects of heavy substance use. Rosenblum and colleagues (1999) used an algorithm to determine whether individuals with co-occurring mood and cocaine use disorders have either an "autonomous" mood disorder—that is, one that either existed prior to the cocaine use disorder or persists during times of abstinence (similar to Schuckit's independent distinction)—or a "nonautonomous" mood disorder that followed from the cocaine use disorder and would remit during cocaine abstinence. Results showed that 27% of subjects were rated as having an autonomous mood disorder, whereas 73% were rated as having a nonautonomous mood disorder.

At this point, differentiating independent from concurrent dual disorders requires significant investment in training interviewers and in interviewing patients. Such requirements often cannot be met in the day-to-day operations of mental health treatment programs. Moreover, multiple assessments may be necessary. For example, Ramsey and colleagues (Ramsey, Kahler, Read, Stuart, & Brown, 2004) examined changes in classifying depressive episodes in alcohol-dependent patients as either

substance-induced depression or independent major depressive disorder. Patients in a partial hospital program for alcohol treatment were assessed five times over a year for symptoms of MDD. Results showed that many (more than 25%) of the cases first categorized as substance-induced MDD were reclassified as independent MDD at some point during the year, owing to depressive symptoms that persisted once the patients had achieved a long period of abstinence.

Implications for Nosology

The fact that two disorders co-occur with great regularity raises the question of whether both categories actually represent two distinct disorders at all (Sher & Trull, 1996). For example, the literature regarding SUDS and ASP finds a high rate of comorbidity between the two disorders, one that is likely enhanced by the symptom overlap inherent in the ASP diagnosis. However, some suggest (Widiger & Shea, 1991) that such a high degree of co-occurrence between these two disorders may mean that these are not, in fact, unique diagnoses, but rather that such a pattern of comorbidity indicates the presence of a single disorder.

IMPACT OF DUAL DIAGNOSIS ON PSYCHOPATHOLOGY RESEARCH

Dual diagnosis affects several areas that are critical to psychopathology research, including diagnosis, sample selection, and interpretation of research findings.

Diagnostic and Sample Selection Issues in Psychopathology Research

An accurate diagnosis is a necessary starting point for any psychopathology study, and dual diagnosis presents an abundance of diagnostic challenges. Individuals with dual diagnoses may provide unreliable diagnostic information, or their data may be inaccurate because of greater severity of impairments. Alternatively, they may minimize their substance use and associated consequences, especially if they have much to lose by admitting to or honestly discussing their substance use, such as services, benefits (Ridgely, Goldman, & Willenbring, 1990), or child custody. The timing of a research diagnostic interview can also impact results, as answers and resulting diagnostic decisions may vary depending on type of use, stage of treatment, and psychiatric stabilization. The method of assessment also can impact diagnostic findings (Regier et al., 1998), and diagnoses given in a clinical setting may vary with those obtained through more structured methods (Fennig, Craig, Tanenberg-Karant, & Bromet, 1994). As presented previously, establishing an accurate diagnosis in individuals with active substance use or withdrawal can be problematic, as the effects of substance use can imitate the symptoms of various psychiatric disorders. Most diagnostic systems used in psychopathology research contend with this difficulty by asking if psychiatric symptoms have been experienced solely during the course of substance use, and may recommend assessment only after a sustained period of abstinence. However, patient reports may be inaccurate, and histories may be too extensive and complicated to allow for this level of precise understanding.

Finally, the issue of overlapping diagnostic criteria can pose a significant difficulty for psychopathology research, as common diagnostic criteria may contribute to the

diagnosis of multiple disorders when in fact the psychopathology is better understood as a single pathological process rather than two distinct disorders (Blashfield, 1990; Sher & Trull, 1996). The overlap of SUDs with ASP is notably problematic, and this frequent comorbidity has long been recognized (Widiger & Shea, 1991). Krueger (1999) examined 10 common mental disorders using structural equation modeling and found that ASP loads onto a common "externalizing" factor along with alcohol and drug dependence, suggesting that substance dependence and ASP may share certain underlying features. Whether this overlap is indeed because of common conceptual characteristics or is an artifact of similar diagnostic criteria is unknown. All of these diagnostic issues impact research findings, in that poor diagnoses will necessarily lead to poor-quality data. Researchers can improve diagnostic reliability by conducting structured interviews, using collateral information and behavioral observation to inform diagnostic decisions, and assessing the patient at multiple time points (Carey & Correia, 1998).

In terms of sample selection, psychopathology and treatment outcome research tends to focus on single or pure disorders and routinely excludes dual diagnosis cases, a practice that has several implications for research. First, screening out dual diagnosis patients yields samples that are atypical. Most patients with one psychiatric disorder meet criteria for some other disorder. Eliminating patients with dual disorders means that the resulting sample is less impaired and less representative of patients who present for treatment, resulting in limited generalizability of research findings (Krueger, 1999). In addition, dual diagnosis patients often have other characteristics that are not adequately represented in the resultant study sample. For example, Partonen, Sihvo, and Lönnqvist (1996) report descriptive data on patients excluded from an antidepressant efficacy that screened out individuals with "chronic alcohol or drug misuse." As a result, younger male patients were likely to be excluded, with current substance abuse as the strongest excluding influence.

Second, dual diagnosis impacts required sample sizes. In their examination of the impact of comorbid disorders on sample selection, Newman and colleagues (1998) discuss findings related to effect sizes of examining only single disorder cases versus the inclusion of dual disorder cases when analyzing group differences. Results showed that when dual disorder cases are excluded, larger sample sizes are required in order to detect small effect sizes. In contrast, retaining dual disorder cases yielded greater variance on study measures, resulting in larger effect sizes requiring smaller sample sizes.

Third, psychopathology and treatment outcome research most often combines those with dual diagnoses together without classification by the specific type of drug use disorder. Whereas some might limit the scope of the study to alcohol only, most cast a wide net and include patients with alcohol, drug, and polysubstance-use disorders. For example, research on substance abuse among patients with severe mental illness typically includes disorders of any number or combination of substances, including alcohol, marijuana, cocaine, and heroin. The impact of grouping all substance use disorders together is unclear, but it certainly raises the possibility that research may miss important issues potentially particular to one substance. For example, it would not be surprising if interventions for patients with a greater number of drug use disorders or with both alcohol and drug use disorders required adaptations that are not necessary for patients with single-drug or alcohol-use disorders.

Similarly, there are likely meaningful differences between patients who inject drugs and those who do not, patients who have long histories of substance dependence and those who do not, or patients who are dependent on cocaine or heroin versus those who are abusing marijuana.

Interpretation of Psychopathology and Treatment Outcome Research

The overall result of screening out those with substance use disorders from psychopathology and treatment outcome research is that there are very few data to inform treatment. For example, following completion of an antidepressant efficacy trial, Partonen and colleagues (1996) point out that they were left without information regarding the efficacy of antidepressants among patients with dual disorders. Given the significant rates of dual disorders found in clinical samples, such an omission is clearly problematic. In their discussion of the many complex issues surrounding comorbidity and psychopathology research, Sher and Trull (1996) question the advantage of studying pure cases when certain disorders occur together with such great frequency that there really may be no ultimate benefit of studying either one alone. It also is unclear how well findings from psychopathology and treatment outcome research will generalize to the larger population of individuals with a particular disorder if patients with dual diagnoses are not included. The epidemiological studies reviewed earlier clearly illustrate that a significant number of those with mental illness or substance abuse experience dual disorders. The relevance of single disorder research to this substantial population of dually impaired individuals is highly suspect, and excluding dual-diagnosis cases yields samples that are not representative of those presenting for treatment.

However, routinely including dual-diagnosis cases in psychopathology and treatment outcome research has its drawbacks. Sher and Trull (1996) and Krueger (1999) discuss the fact that if dual diagnosis cases are included in psychopathology research, understanding of both mental and substance use disorders is compromised, in that samples would be less well-defined. As a result, it would be unclear whether results could be attributed to the disorder under study or to comorbid disorders represented in the sample. In addition, comorbidity complicates longitudinal data because different patterns of comorbidity may emerge over time within individuals (Sher & Trull, 1996). One possible strategy for dealing with dual disorders in psychopathology and treatment outcome research is the use of samples that include comorbid cases in percentages found in the general population in order to increase the generalizability of findings (Newman et al., 1998; Sher & Trull, 1996). Widiger and Shea (1991) offer additional options, including having one diagnosis take precedence over another, adding criteria in order to make a differential diagnosis, or removing criteria shared by disorders. Sher and Trull (1996) additionally suggest statistically controlling for comorbidity via regression techniques but acknowledge that this practice can mask important common features of disorders.

THEORIES OF DUAL DIAGNOSIS

This review makes two points clear: Dual diagnosis is highly prevalent, and it has a pervasive impact on both clinical and research domains. There now is general

agreement that the time has come to define more precisely the mechanisms underlying dual diagnosis, which is a complex task for several reasons. Most important, there is a great degree of heterogeneity found in dual diagnosis populations. The numerous types of psychopathological disorders and substances of abuse ensure many dual diagnosis combinations. In addition, although the term *dual* is meant to describe cases with both mental illness and substance use problems, it can in actuality reflect more than two disorders (for example, an individual might meet criteria for an affective disorder, an anxiety disorder, and a substance use disorder). Thus, it is unlikely that one explanation or causal model for dual diagnosis can explain the diversity of cases and experiences that are found.

Models to explain dual diagnoses tend to fall into one of four general categories (see Mueser, Drake, & Wallach, 1998, for a review). Third variable or common factors models suggest that some shared influence is responsible for the development of both psychiatric and substance use disorders. The two types of causal models—secondary substance use disorder models and secondary psychiatric disorder models—posit that either type of disorder causes the other. Bidirectional models suggest that either psychiatric or substance use disorders can increase risk for and exacerbate the impact of the other. These models have been more or less described depending on the particular area of psychopathology. Examination of this literature finds that models of dual diagnosis are typically organized by disorder, with research focused on specific combinations of dual disorders rather than on the issue of dual diagnosis across disorders. Extensive reviews of models in each of these categories can be found (Blanchard, 2000; Mueser et al., 1998). The following section provides a review of some models of dual diagnosis in their respective domains of psychopathology.

COMMON FACTORS MODELS

Common factors models suggest a shared etiological basis for psychiatric and substance use disorders. Most research has focused on genetics as the likely common factor. Results of numerous twin, adoption, and family studies clearly show that both mental illness and substance abuse run in families, and that familial aggregation of single disorders is substantial (Kendler et al., 1997; Kushner et al., 1990; Merikangas et al., 1985; Merikangas & Gelernter, 1990). Such findings have led to the hypothesis that commonly co-occurring disorders might be linked via common genetic factors. However, for genetics to serve as a viable common factor, family studies must show high rates of transmission of pure forms of both substance use and psychiatric disorders. For example, a proband with depression only should have an increased rate of alcoholism only in the individual's relatives in order to provide evidence of shared genetic etiology.

Studies of familial transmission of a range of comorbid psychiatric and substance use disorders find that the evidence for a common genetic factor is lacking. Merikangas and Gelernter (1990) reviewed family, twin, and adoption studies of alcoholism and depression and concluded that familial transmission of pure forms of the disorders was not supported: "Depressed only" probands did not have increased rates of "alcoholism only" in their relatives, and "alcoholism only" probands did not have increased rates of "depression only" in their relatives. These authors stress that although familial aggregation of disorders is evident, the notion of a common genetic

factor underlying the two is not supported, and the disorders appear to be transmitted separately.

In subsequent analyses of familial transmission of comorbid depression and substance use disorders using data from the Yale Family Study of Comorbidity of Substance Disorders, Swendsen and Merikangas (2000) similarly found that there was no support for a common factors model: Mood disorders in the proband were not associated with an increased risk of alcohol dependence in relatives. Similar results have been reported with schizophrenia (Kendler, 1985), ASP (Hesselbrock, 1986), and patients with schizoaffective and bipolar disorders (Gershon et al., 1982).

Importantly, common factors other than genetics may exist. Several possible common factors might link substance use disorders and severe mental illness, including comorbid ASP, low socioeconomic status, and poor cognitive functioning (Mueser et al., 1998). For example, ASP is associated with both substance use disorders and severe mental illness. Mueser and colleagues (1999) examined the links between conduct disorder, ASP, and substance use disorders in patients with severe mental illness and found that both childhood conduct disorder and adult ASP were significant risk factors for SUDs. However, the status of ASP as a risk factor is unclear, given that problem substance use is part of the diagnosis of ASP, raising the possibility that ASP may be a byproduct of substance use disorder. Also, ASP is based in large part on criminality and socioeconomic status, both of which are difficulties that often go along with both substance use disorder and severe mental illness (Mueser et al., 1998).

Other researchers are proposing multivariate approaches to identifying common factors of dual disorders. One such model is described by Trull and colleagues (2000) to explain the high prevalence of dual substance use disorders and borderline personality disorder. These authors suggest that a family history of psychopathology inspires both dysfunctional family interactions and the inheritance of deviant personality traits that are associated with the development of both borderline personality disorder and substance use disorders. Specifically, the personality traits of affective instability and impulsivity are central to both disorders and are conceptualized as stemming from a combination of "constitutional and environmental factors" (Trull et al., 2000) that include inherited deficiencies in serotonergic functioning, in combination with a deviant family environment that may include associated childhood trauma. These factors in turn impact the development of borderline personality disorder and SUD, both alone and in combination. These authors stress that although this model is currently speculative, more prospective, longitudinal studies with a developmental and multivariate focus will enable the pieces of the models to be evaluated simultaneously. This model provides an example of combining strategies from family studies and psychopathology research into a multivariate framework that provides rich details as to how two disorders could be developmentally related.

In fact, the description and measurement of multivariate influences in the development and maintenance of dual disorders are becoming increasingly sophisticated, spanning from neurophysiology to postnatal development factors such as family stress (Fishbein & Tarter, 2009). Several studies have focused on the identification of neurocognitive and neurophysiological vulnerability indicators for substance use and psychiatric disorders. The P3 event-related potential (ERP) is a neurophysiological measure of brain activity that occurs between 300 and 600 milliseconds after stimulus presentation and is implicated in cognitive information processing, response

inhibition, and self-regulation (Begleiter & Porjesz, 1995; Fishbein & Tarter, 2009). Reduced P3 amplitude has been fairly consistently identified among individuals with an alcohol SUD who are abstinent, as well as in populations at high risk for SUD (e.g., sons of fathers with alcohol dependence) suggesting that it is a heritable preexisting vulnerability marker, or endophenotype, for alcohol use disorders (Begleiter & Porjesz, 1995).

As discussed previously, conduct disorder or, more generally, externalizing disorders often co-occur with SUDs. Reduced P3 has also been associated with externalizing disorders (e.g., ADD; Klorman, 1991), which suggests it may represent a common factor to both of these disorders (Iacono, Carlson, Malone, & McGue, 2002). In a large longitudinal community-based sample, Iacono and colleagues (2002) measured P3 amplitude and assessed for a series of disorders including attention-deficit/hyperactivity disorder, conduct disorder, ASP, and SUD in a sample of 502 male adolescents and their parents. Participants were assessed at age 17 and then reassessed 3 years later. Results indicated that reduced P3 amplitude was associated with not only a paternal history of SUD but also paternal history of ASP. It was also associated with childhood disorders of disinhibition including SUDs, and P3 amplitude at age 17 predicted the development of several disorders of disinhibition including SUD. The authors conclude that reduced P3 amplitude may be a common, genetically transmitted risk factor for a broad range of psychiatric disorders including SUD that share the common feature of behavioral disinhibition. It is anticipated that with continued advancements in cognitive neuroscience, similar endophenotypes will be identified that will facilitate the identification of common genetic risk factors for dual disorders.

Secondary Substance Abuse Models

Secondary substance abuse models contend that mental illness increases vulnerability to SUDs. Probably the most widely discussed model of this type is the self-medication model, which asserts that individuals with psychiatric disorders use substances as a way to self-medicate psychopathological symptoms and relieve discomfort associated with the primary psychiatric disorder.

There are several types of studies used to examine applicability of a self-medication model to different forms of psychopathology. Some determine the ages of onset of dual disorders, with the idea being that SUDs developing after other Axis I psychopathology support the self-medication hypothesis. Some examine subjective reasons for use among patients with different disorders, while others correlate levels of symptoms with levels of substance abuse (from a self-medication perspective, greater symptoms should correlate with greater substance abuse). Another line of self-medication research involves investigating the types of substances used by different patient groups. According to a self-medication hypothesis, patients with certain psychopathological conditions should preferentially seek out and use substances that will directly impact symptoms associated with their specific psychopathology.

Support for a self-medication model varies depending on the type of mental illness under investigation. For example, although the model is popular among treatment providers working with patients with severe mental illness, empirical support for a self-medication model has not been compelling (see Mueser et al., 1998, for a review).

Although it has been suggested that schizophrenia patients preferentially abuse stimulants to self-medicate negative symptoms (Schneier & Siris, 1987), this finding has not been replicated in other studies (Mueser, Yarnold, & Bellack, 1992). Most important, studies fail to find evidence that specific substances are used in response to specific symptoms. Rather, patterns of drug use appear to be strongly associated with demographic factors and drug availability (Mueser, Yarnold, et al., 1992). In addition, a self-medication model of SUDs in severe mental illness would predict that the more symptomatic patients would be at higher risk for substance use disorders (Mueser, Bellack, et al., 1992). Several studies, however, have found the opposite to be true: More severely ill patients are less likely to abuse substances (Chen et al., 1992; Cohen & Klein, 1970; Mueser, Yarnold, et al., 1992), and patients with SUDs have better premorbid social functioning (Dixon et al., 1991).

Although individuals with schizophrenia and other severe mental illnesses report a range of reasons for substance use—to alleviate social problems, insomnia, or depression; to get high; to relieve boredom; and to increase energy—few endorse using specific substances to combat particular psychiatric symptoms (see Brunette, Mueser, Xie, & Drake, 1997, for a review). Moreover, many studies have found that patients with schizophrenia report worsening of symptoms with substance abuse, including increased hallucinations, delusions, and paranoia (Barbee et al., 1989; Cleghorn et al., 1991; Dixon et al., 1991; Drake et al., 1989), and others have found that more severe symptoms of schizophrenia are not linked to more severe substance abuse (Brunette et al., 1997). Similarly, findings of increased rates of cocaine use among patients with bipolar disorder, interpreted by some to indicate self-medication of depressive symptoms, have been found upon review to more likely reflect attempts to prolong euphoric feelings associated with mania (Goodwin & Jamison, 1990).

Other secondary substance abuse models may be more relevant to patients with severe mental illness. A social facilitation model suggests that patients with severe mental illness may have fewer available opportunities for social interaction, and that substance abuse helps smooth the process of social engagement in patients who lack appropriate social and interpersonal skills. Finding that a large portion of substance use/abuse by individuals with schizophrenia occurs in a public setting, Dixon, Haas, Weiden, Sweeney, and Frances (1990) suggest that drug use may provide "isolated, socially handicapped individuals with an identity and a social group" (p. 74) or to fulfill needs for contact and acceptance (Mueser, Bellack, et al., 1992).

Others offer an alleviation of dysphoria model; substance abuse represents an attempt to alleviate these negative mood states. Evidence for self-medication may be more relevant to dual diagnosis within other psychopathological disorders. For example, several reviews have found that self-medication may apply to dual PTSD and SUDs, especially among women with trauma-related PTSD. Three main theories (Chilcoat & Breslau, 1998) are (1) the self-medication hypothesis, which suggests that drugs are used to medicate PTSD symptoms; (2) the high-risk hypothesis, which suggests that drug use puts individuals at heightened risk for trauma that can lead to PTSD; and (3) the susceptibility hypothesis, which suggests that drug users are more likely to develop PTSD following exposure to a traumatic event. They then use data from a sample of more than 1,000 young adults who were randomly selected from enrollees in a large health maintenance organization and were followed longitudinally over 5 years in order to examine the timing of the development of both PTSD and

substance use disorders. Those with a history of PTSD at baseline were 4 times more likely than those without PTSD to develop drug abuse or dependence at some point during the 5 years of the study. In contrast, baseline drug abuse/dependence did not confer any increased risk of subsequent exposure to trauma or to developing PTSD in those who did experience some traumatic event during the follow-up period.

Other data on dual SUD and PTSD (Stewart et al., 1998) that also lend support to a self-medication model include: (a) development of substance abuse most often follows development of PTSD; (b) patients often report that they perceive substance use to be effective in controlling PTSD symptoms; (c) patients with both PTSD and substance use disorder report more severe trauma and a greater severity of PTSD symptoms, suggesting that substances are used in an effort to control greater psychiatric symptomatology; and (d) drugs of abuse may be related to different clusters of PTSD symptoms, suggesting that substance abuse may be linked to attempts to control intrusion or arousal symptoms of PTSD. These authors stress that although a self-medication model is likely too simplistic to explain all forms of PTSD–SUD comorbidity, at this point it provides a good fit for the current literature.

Recently there has been increased interest in neurobiological mechanisms that underlie dual diagnosis, particularly with respect to the ways in which mental illness and addiction share common neurological pathways. The foundation for this research is that neurobiological deficits and abnormalities that provide the basis for different forms of mental illness may predispose those with mental illness to substance abuse.

This literature includes animal studies of dual diagnosis, where brain lesions are produced to simulate different forms of psychopathology. Factors such as the ability to experience reinforcement from drug use and differential patterns of use and/or cravings are examined. A good summary of this approach to dual diagnosis in schizophrenia is presented by Chambers, Krystal, and Self (2001). Briefly, increased vulnerability to substance use disorders in schizophrenia results from impairment in brain systems that are central to schizophrenia—the most important of which may be the mesolimbic dopamine system (MDS). According to this model, the MDS is implicated in the reinforcing effects of drug use (drug use increases dopamine levels), as well as in the development of schizophrenia (high dopamine levels are implicated as a major factor in the development of schizophrenia). In other words, these authors suggest that the neuropathology of schizophrenia may contribute to the vulnerability to addiction by facilitating neural substrates that mediate positive reinforcement. The putative neuropathology underlying schizophrenia involves alterations in neuroanatomic circuitry that regulate positive reinforcement, incentive motivation, behavioral inhibition, and addictive behavior (Chambers et al., 2001, p. 71).

Thus, the neurobiological problems that give rise to schizophrenia also put the individual at heightened risk for developing SUDs. Several studies have found support for this sort of neurological linkage in schizophrenia. Chambers and Self (2002) studied rats with neonatal ventral hippocampal lesions (NVHL rats), a procedure that produces behavioral disturbances in rats that resemble the psychopathological behaviors seen in schizophrenia, including positive and negative symptoms and abnormal cognitive functioning (see Chambers & Self, 2002, and Chambers & Taylor, 2004, for details of the procedure and its effects). In comparison to controls (rats with sham lesions), NVHL rats showed faster rates of cocaine self-administration, higher degree of binge cocaine use, and faster relapse to cocaine use

following a period of nonuse. Other studies using this and similar methodologies have generated similar findings (Chambers & Taylor, 2004).

Similar animal models are available for depression and substance use. In one model for depression, rats undergo bilateral olfactory bulbectomy (OBX), creating behavior that is biologically and behaviorally similar to depression in humans, including decreased pleasure seeking, disruptions in sleep, agitation, and other cognitive problems that respond only to chronic (and not acute) antidepressant treatment (see Holmes et al., 2002, for a thorough review). Importantly, this procedure also causes dopamine dysregulation in areas of the brain implicated in the reinforcing effects of drugs of abuse, again similar to those found in humans. In comparison to rats with sham lesions (Holmes et al., 2002), those with OBX lesions were more sensitive to the reinforcing effects of amphetamine. Specifically, they learned to self-administer amphetamine more quickly and had higher levels of stable amphetamine administration.

Other studies have used rats genetically bred for signs of learned helplessness as an operational definition of depression in rats. For example, Vengeliene and colleagues (Vengeliene, Vollmayr, Henn, & Spanagel, 2005) examined differences in alcohol intake between congenital learned helplessness rats (cLH) and congenital nonlearned helplessness rats (cNLH)—two lines of rats selectively bred for different escape reactions following inescapable shock (cLH rats do not try to escape the shock, even though they have not been exposed to it before, whereas cNLH rats will try to escape the shock). In this study, these two groups of rats were given access to alcohol and tap water for self-administration for 6 weeks and then underwent 2 weeks of no alcohol access followed by renewed access to alcohol for 4 days. Although results showed no differences in males, female cLH rats consumed greater amounts of alcohol than cNLH rats during the self-administration portion of the study and showed a more pronounced alcohol deprivation effect (greater consumption of alcohol following a period with no alcohol consumption). The authors suggest that inborn "depressive-like" behavior in female rats is associated with increase alcohol intake. These and other animal models of depression (Fagergren, Overstreet, Goiny, & Hurd, 2005) appear to be a useful avenue for the study of dual diagnosis involving depression and substance abuse. Such studies are finding that "depressed" animals respond differently than other animals to drugs and alcohol, providing interesting new leads in the search for biological mechanisms that lead to dual diagnosis.

The high rate of smoking among individuals with schizophrenia is another possible instance in which a neurophysiological deficit predisposes individuals to engage in substance use. Rates of smoking among individuals with schizophrenia are exceedingly high when compared to the general population (de Leon et al., 1995; Hughes, Hatsukami, Mitchell, & Dahlgren, 1986). Individuals with schizophrenia tend to smoke more cigarettes (de Leon et al., 1995), smoke higher nicotine content cigarettes, and smoke harder in an attempt to extract higher doses of nicotine from cigarettes (Olincy, Young, & Freedman, 1997).

Somewhat different than the self-medication of symptoms of schizophrenia discussed previously, intriguing data suggest that, for some individuals with schizophrenia, smoking may be an attempt to adapt to a neurophysiological deficit related to sensory gating. Specifically, Adler, Hoffer, Wiser, and Freedman (1993) investigated the impact of cigarette smoking on the P50 ERP. This ERP is involved in habituation to

stimuli and functions to screen out irrelevant information. It is typically elicited with a sensory gating paradigm where two auditory clicks are presented in close temporal sequence. In intact sensory gating there is a diminished neurophysiological response to the second click. Functionally, this represents a screening out of less relevant information, thus allowing for the availability of more cognitive resources for the processing of new salient stimuli.

Consistent with other research, Adler et al. (1993) found that in the case of individuals with schizophrenia, there is a failure to inhibit the response to the second click. However, when allowed to smoke freely, there was a normalization (i.e., greater inhibition in response to the second click), albeit lasting only briefly. In a second experiment, Adler, Hoffer, Griffith, Waldo, and Freedman (1992) investigated the impact of nicotine gum in first-degree relatives of individuals with schizophrenia who were nonsmokers and had a demonstrated sensory gating deficit (as measured by P50). Results were similar to the patient sample: Relatives demonstrated a transient improvement in P50 ERP. Interestingly, these effects were only found with a higher dose of nicotine gum (6 mg); pilot testing with lower doses failed to yield an effect (Adler et al., 1992).

Another well-documented psychophysiological deficit in individuals with schizophrenia that has also been identified in first-degree relatives is that of eye tracking dysfunction, namely smooth pursuit eye movement (SPEM; e.g., Holzman, 1987). Briefly, when required to visually track a moving object, impaired individuals demonstrate an increase in "catch-up" (due to tracking too slowly) and "leading" eye saccades (due to tracking too quickly or visually "jumping" ahead of the stimuli; Olincy, Ross, Young, Roath, & Freedman, 1998). Essentially, these saccades decrease the accuracy and efficiency with which individuals visually track a moving object. Olincy et al. (1998) found that in individuals with schizophrenia, performance on a SPEM task significantly improved when patients were allowed to smoke freely (compared to task performance after a 10-hour period of abstinence from smoking).

Notably, after smoking, there was a significant decrease in leading saccades, which the authors postulated was an indication of enhanced inhibition and similar to nicotine's normalizing effect in the P50 ERP. These neurophysiological findings have been linked to the alpha-7 nicotinic receptor, a low-affinity receptor that requires high doses of nicotine for activation, which may partially explain heavy smoking (i.e., extracting higher doses of nicotine) among individuals with schizophrenia (Adler et al., 1998). In addition to furthering our understanding of the impact of nicotine on the pathophysiology of schizophrenia, these findings have also helped contribute to the development of new cognitive-enhancing medications for individuals with the disorder (e.g., Olincy et al., 2006).

Secondary Psychiatric Disorder Models

With some specific differences, these models suggest that substance abuse causes psychopathology. Schuckit and Monteiro (1988; Schuckit, 1983) stress that the use of or withdrawal from many psychoactive substances causes reactions that appear indistinguishable from psychiatric disorder. As reviewed earlier, these authors contend that substance use disorders are often mistakenly diagnosed as psychiatric disorders because of similar symptomatology, and that, although serious

psychopathology can be expected in the course of substance use disorder, substance-induced disorders are likely to remit following several weeks of abstinence.

The case for substance-induced psychiatric disorder appears to be particularly relevant to dual SUDs and major depression. Raimo and Schuckit (1998) review the evidence in support of the idea that most cases of comorbid depression and alcohol dependence are substance-induced, including findings that (a) drinking can cause severe depressive symptoms; (b) treatment-seeking substance abusers show increased rates of depression that often remit following abstinence and in the absence of specific treatments for depression; (c) individuals with substance-induced depression do not show elevated rates of depression in family members; and (d) children of alcoholics show higher rates of alcohol use disorders but do not show elevated rates of major depression. These authors stress that, although having independent depression in addition to alcohol abuse or dependence is certainly possible, most of the depression that is comorbid with alcohol use disorders is substance-induced and not independent in nature.

Following this example, Swendson and Merikangas (2000) reviewed findings that are relevant to an etiological model of dual substance abuse and depression: (a) The onset of alcohol dependence typically precedes the onset of unipolar depression; (b) symptoms of depression often remit following several weeks of abstinence from alcohol; and (c) genetic studies do not support a shared genetic basis for comorbidity of depression and alcohol dependence. They suggest that the association between unipolar depression and alcohol dependence may best be described via a secondary psychiatric disorder model, in which chronic alcohol use causes unipolar depression, through either the considerable life stress that alcohol dependence promotes for the drinker in many important domains of functioning, or through the pharmacological properties of alcohol as a depressant substance.

Bidirectional Models

Bidirectional models propose that ongoing, interactional effects account for increased rates of comorbidity. Support for a bidirectional model for anxiety and alcohol dependence (Kushner, Abrams, & Borchardt, 2000) includes the following: (a) most patients with anxiety and alcohol use disorders report drinking to control fears and reduce tension; (b) drinking can cause anxiety (i.e., anxiety can result from long-term alcohol use, patients report increased anxiety after drinking, and withdrawal from alcohol can cause physiological symptoms of anxiety); (c) alcohol dependence can lead to anxiety disorders (i.e., alcohol dependence puts one at increased risk for later development of an anxiety disorder, and chronic drinking can cause neurochemical changes that cause anxiety and panic); and (d) anxiety disorders can lead to alcohol dependence (i.e., having an anxiety disorder puts one at increased risk for later development of alcohol dependence, alcohol provides stress-response dampening and reduces the clinical symptoms of anxiety, and many people use alcohol to self-medicate anxiety symptoms).

The authors conclude that alcohol and anxiety interact to produce an exacerbation of both anxiety symptoms and drinking. Whereas initial use of alcohol provides short-term relief of anxiety symptoms, it negatively reinforces further drinking, leading to increased physiological symptoms of anxiety. They then propose a so-called feed-

forward cycle wherein drinking is promoted by its short-term anxiety-reducing effects of alcohol, whereas anxiety symptoms are worsened by heavy drinking, leading to continued drinking in response to these worsened anxiety symptoms.

Although several caveats and issues remain to be clarified (i.e., the model seems to best fit with comorbid alcohol dependence and its relevance to drug use disorders is unknown; those for whom the anxiety disorder begins first would not necessarily experience the anxiety-reducing properties of alcohol in a way that would initiate the feed-forward cycle), the authors suggest that a bidirectional model can best explain existing findings and can focus future research on comorbidity of anxiety and substance use disorders. Moreover, this sort of bidirectional model highlights the possibility that unidirectional causal models are likely too simplistic an approach in explaining comorbidity. Rather, the relationship between psychiatric and substance use disorders is more likely characterized by complex interactions between the two disorders.

SUMMARY AND FUTURE DIRECTIONS

We are at a critical juncture in the field of dual diagnosis and its impact both clinically and in research. Over the past three decades, efforts have focused primarily on identifying the problem of dual diagnosis—including its rates and consequences—and getting clinicians and researchers to think about dual disorders when pursuing their clinical or research work. We have learned much about the prevalence and impact of dual disorders from general population and clinical studies over the last several decades.

Currently we can say with certainty that dual diagnosis is common, both in the general population and among clients in mental health and substance abuse treatment. Comorbid psychiatric and substance use disorders impact a large percentage of people, and dual disorders persist over time. These patterns are likely to shift as a broadened definition of substance use disorder that routinely includes tobacco dependence makes its way into the mainstream of thinking around dual diagnosis. It will be interesting to see how the new definitions and conceptualizations that are part of *DSM-5* impact dual diagnosis. As noted previously, changes in the diagnosis of substance use disorders that include merging abuse and dependence into one disorder, the addition of gambling disorder, and changes to the diagnostic requirements for other disorders could lead to higher rates of dual diagnosis. Individuals with less severe problems (abuse) who may have been overlooked or not included previously may now be counted.

Importantly, we are now beginning to see that patients who present with multiple diagnoses are the most difficult and complex patients to understand and treat. The notion of dual disorders may require reconceptualization as the frequency of individuals with two, three, or more comorbid psychiatric and substance use disorders continues to climb. Such findings highlight the potential need to adjust our thinking about *dual* diagnosis and whether the term should be updated from *dual* to *multiple* as a way to more accurately capture the reality that many cases of dual diagnosis really reflect multiple comorbid conditions.

The issue of multiple comorbidities—multiple substance use, psychiatric, and even medical disorders within individuals—is probably the most critical issue facing

assessment and diagnosis of dual disorders. Research is starting to examine the interrelationships among mental health, somatic disease, and addiction. The inclusion of tobacco dependence within the framework of dual diagnosis plays an important role in this shift. For example, work on the relationships among mood disorders, smoking and tobacco dependence, and the presence of and recovery from physical illnesses such as heart disease is finding complex associations that impact treatment, recovery, and relapse (Stafford, Berk, & Jackson, 2013). Findings that individuals with mental health disorders have more health risk factors such as diabetes, obesity, and smoking but receive less medical treatment for them (Briskman, Bar, Boaz, & Shargorodsky, 2012) highlight the need for more attention to the public health impacts of multiple comorbidities.

Second, it is clear that research on psychopathology and its treatments is complicated by questions of dual diagnosis. Dual diagnosis impacts basic questions of research methodology and impact: Who is included and excluded in dual diagnosis research? How are dual disorders handled in data collection and analysis? How are research findings to be understood when individuals have multiple disorders? Although acknowledging and adapting to the reality of multiple comorbidites within individuals will further complicate treatment research, it is essential that research explore ways to include and be applicable to individuals with multiple conditions. That is, it is increasingly less useful to explore the relationships between only two disorders, or to limit the development of treatments to individuals with two disorders, when many of those with comorbid conditions have more than two problems. Practically speaking, issues of mood, anxiety, and substance use are intertwined for many people, and research will need to address the understanding and treatment of these syndromes together rather than separately.

Finally, several models that explain dual diagnosis take into account the different types of psychopathology and substances of abuse, as well as the differences in disorder severity. Research linking neurobiological development of psychiatric disorders to substance abuse vulnerability highlights the need to incorporate biological and psychological constructs as we proceed in trying to understand dual diagnosis. The next step is to further examine causal mechanisms and determine how these models work given the significant heterogeneity seen in the dual diagnosis population. Although a range of theories has been proposed, more specific work is required to fully examine the links between mental illness and substance use disorders. Here again, research will have to adapt to the current reality of multiple comorbidities. At present it is unclear how prevailing models of dual disorders that are organized around a pair of problems are going to be relevant to individuals with three or more diagnoses. Overall, moving forward in our understanding of dual disorders will require that we focus on comorbidity and the connections among multiple problems as a way to best learn about and treat individuals.

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CHAPTER 3

Structured and Semistructured Interviews for Differential Diagnosis

Fundamental Issues, Applications, and Features

DANIEL L. SEGAL and KADIJA N. WILLIAMS

STRUCTURED AND SEMISTRUCTURED interviews were developed to address the difficulties that clinicians and researchers historically have had in making accurate diagnoses of mental disorders with traditional unstructured clinical interviews. A major contributing factor to diagnostic imprecision was the lack of uniformity or standardization of questions asked of respondents to evaluate the nature and extent of their psychiatric symptoms and to arrive at a formal diagnosis. Structured and semistructured interviews solve this problem by their very nature. As such, they have become increasingly popular and effective in the mental health field, leading to vastly improved diagnostic clarity and precision. The purpose of this chapter is to provide a basic introduction to structured and semistructured interviews used to assess and diagnose psychopathology among adults. We begin with a discussion of the basic types of applications of structured and semistructured interviews followed by an exploration of their major features, advantages, and drawbacks. We conclude this chapter with a discussion of the most popular multidisorder structured and semistructured interviews used to diagnose clinical disorders and personality disorders.

With the recent publication of the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (*DSM-5*; American Psychiatric Association [APA], 2013), many changes have occurred, especially regarding the classification and organization for many clinical disorders. One major change was the removal of the multiaxial system, which previously denoted an important distinction between clinical disorders and personality disorders on separate diagnostic axes. Notably, no changes were made to the classification and diagnostic criteria for the personality disorders. In this chapter, we describe the anticipated changes to some of the major structured and semistructured interviews as these measures become updated from their linkage to the *DSM-IV-TR* (APA, 2000) to the *DSM-5*.

BASIC ISSUES REGARDING STRUCTURED AND SEMISTRUCTURED INTERVIEWS

The most common method among mental health professionals to evaluate and diagnose their clients is the direct clinical interview (Segal & Hersen, 2010). Such interviews, however, can vary tremendously, especially regarding the amount of *structure* that is imposed. Indeed, some important differences exist between less structured interviews and more structured ones. Unstructured clinical interviews are dependent on the clinician's unique background, knowledge base, theoretical model, and interpersonal style, and thus are highly flexible. Within this unstructured approach, clinicians are entirely responsible for asking whatever questions they decide are necessary to reach a diagnostic conclusion. In fact, any type of question or topic (relevant or not) can be pursued in any way that fits the mood, preferences, training, specific interests, or philosophy of the clinician. As a consequence, one can imagine the variability across interviews from one clinician to another. On the other hand, structured interviews conform to a standardized list of questions (including follow-up questions), a uniform sequence of questioning, and systematized ratings of the client's responses. These questions are designed to measure the specific criteria for many mental disorders as presented in the *DSM*. These essential elements of structured interviews serve several important purposes, most notably that their use:

- Increases coverage of many mental disorders that otherwise might be overlooked.
- Enhances the diagnostician's ability to accurately determine whether particular symptoms are present or absent.
- Reduces variability among interviewers, which improves reliability.

These features of structured interviews add much in developing clinical psychology into a true science. For example, structured interviews are subject to evaluation and statistical analysis, and they can be modified and improved based on the published literature regarding their psychometric properties.

Not all structured interviews are the same. In fact, the term *structured interview* is broad, and the actual amount of structure provided by an interview varies considerably. Structured interviews can be divided into one of two types: *fully structured* or *semistructured*. In a fully structured interview, questions are asked verbatim to the respondent, the wording of probes used to follow up on initial questions is specified, and interviewers are trained to not deviate from this rigid format. In a semistructured interview, although initial questions for each symptom are specified and are typically asked verbatim to the respondent, the interviewer has substantial latitude to follow up on responses. The interviewer can modify or augment the standard inquiries with individualized and contextualized probes to more accurately rate specific symptoms. The amount of structure provided in an interview clearly impacts the extent of clinical experience and judgment that are required to administer the interview appropriately: Semistructured interviews require clinically experienced examiners to administer the interview and to make diagnoses, whereas fully structured interviews can be administered by nonclinicians who receive training on the specific instrument. This latter difference makes fully structured interviews popular and economical, especially in large-scale research studies in which accurate diagnoses are essential.

Structured and semistructured interviews have been created to assist with the differential diagnosis of all major clinical disorders (formerly defined on Axis I of the *DSM-IV*) and all standard personality disorders (formerly defined on Axis II of the *DSM-IV*). Interviews used for psychiatric diagnosis are typically aligned with the *DSM* system and, therefore, assess the formal diagnostic criteria specified in the manual. However, structured interviews exist beyond those designed for *DSM* differential diagnosis. Other structured interviews are narrower in focus; for example, to assess a specific problem or form of psychopathology (e.g., eating disorders, substance abuse, borderline personality disorder features) in great depth. An excellent resource for information about a host of specialized interviews is provided by Rogers (2001). Our focus now turns to a discussion of some common functions of structured and semistructured interviews.

APPLICATIONS OF STRUCTURED AND SEMISTRUCTURED INTERVIEWS

Whereas structured and semistructured interviews are used in many different venues and for many different purposes, their application falls into three broad areas: research, clinical practice, and clinical training.

Research. The research domain is the most common application, in which structured or semistructured interviews are used to formally diagnose participants for inclusion into a study so that etiology, comorbidity, and treatment approaches (among other topics) can be explored for a particular diagnosis or group of diagnoses. Sound empirical research on mental disorders certainly requires that individuals assigned a diagnosis truly meet full criteria for that diagnosis. Another research application for structured interviews is to provide a standardized method for assessing change in one's clinical status over time. As noted by Rogers (2003), these types of longitudinal comparisons are essential for establishing outcome criteria, which is vital to diagnostic validity.

Clinical Practice. In clinical settings, administration of a structured or semistructured interview may be used as part of a comprehensive and standardized intake evaluation. Routine and complete administration of a structured interview is increasingly common in psychology training clinics, but doing so requires considerable training for clinicians and time for full administration. A variation on this theme is that sections of a structured interview may be administered subsequent to a traditional unstructured interview to clarify and confirm the diagnostic impressions. Widiger and Samuel (2005) provide another thoughtful alternative especially regarding the assessment of personality disorders in clinical practice. They recommend the strategy of administering an objective self-report inventory, which is followed by a semistructured interview that focuses on the personality disorders that received elevated scores from the testing. This strategy is responsive to time constraints in clinical practice but also allows for collection of standardized, systematic, and objective data from the structured interview. Finally, we wish to emphasize that in clinical settings, structured interviews should not take the place of traditional clinical interviews. Both can be performed, although at different times and for different purposes. The combination of the two approaches, integrated flexibly to meet the needs of the individual clinician and his or her clients, reflects the best of the scientist-practitioner model in which the science and art of assessment are both valued and valuable (Rogers, 2003).

Clinical Training. Use of structured or semistructured interviews for training mental health professionals is an increasingly popular and ideal application, because interviewers have the opportunity to learn (through repeated administrations) specific questions and follow-up probes used to elicit information and evaluate specific diagnostic criteria provided by the *DSM*. Modeling the questions, sequence, and flow from a structured interview can be an invaluable source of training for beginning clinicians.

ADVANTAGES AND DISADVANTAGES OF STRUCTURED AND SEMISTRUCTURED INTERVIEWS

No assessment device in the mental health field is perfect, and structured and semistructured interviews are no exception to this truism. In this section, the strengths and weaknesses of structured interviews are discussed. Our intention is to give readers an appreciation of the major issues to be considered when deciding whether to use the structured interview approach to assessment. A brief summary of the advantages and disadvantages is presented in Table 3.1.

Advantage: Increased Reliability Perhaps the most important advantage of structured interviews centers on their ability to increase diagnostic reliability (reliability defined in this context refers to consistency or agreement about diagnoses assigned by

Table 3.1
Advantages and Disadvantages of Structured and Semistructured Interviews

Advantages	Disadvantages
Increased Reliability: Because questions are standardized, structured interviews decrease variability among interviewers, which enhances interrater reliability. Structured interviews also increase the reliability of assessment for a client's symptoms across time, as well as the reliability between client report and collateral information.	**May Hinder Rapport:** Use of structured interviews may damage rapport because they are problem-centered, not person-centered, and poorly trained interviewers may neglect to use their basic clinical skills during the assessment.
Increased Validity: Structured interviews assure that diagnostic criteria are covered systematically and completely. This is important because it serves to increase the validity of diagnosis.	**Limited by the Validity of the Classification System Itself:** Structured interviews used for diagnosis are inherently tied to diagnostic systems. Thus, they are only as valid as the systems upon which they are based. Furthermore, it is difficult to establish the validity of particular structured interviews because there is no gold standard in psychiatric diagnosis.
Utility as Training Tools: Structured interviews are excellent training tools for clinicians in training because structured interviews promote the learning of specific diagnostic questions and probes used by experienced clinical interviewers. In addition, nonclinicians can easily be trained to administer fully structured interviews, which can be cost effective in both research and clinical settings.	**The Trade-Off of Breadth Versus Depth:** Structured interviews are limited because they cannot cover all disorders or topic areas. When choosing a structured interview, one must evaluate carefully the tradeoffs of breadth versus depth of assessment.

different raters; Coolidge & Segal, 2010a). By systemizing and standardizing the questions interviewers ask, and the way answers to those questions are recorded and interpreted, structured interviews decrease the amount of information variance in diagnostic evaluations (e.g., Rogers, 2001). That is, structured interviews decrease the chances that two different interviewers will elicit different information from the same client, which may result in different diagnoses. Thus, interrater reliability, or the likelihood that two different interviewers examining the same individual will arrive at the same diagnosis, is greatly increased.

Increased interrater reliability has broad implications in clinical and research settings. Because many psychological and psychopharmacological treatments are intimately tied to specific diagnoses, it is imperative that those diagnoses be accurate (Segal & Coolidge, 2001). Thus, if different clinicians interviewing the same client arrive at different diagnostic conclusions, it would be challenging to make a definitive decision about treatment. Similarly, accurate diagnosis is also essential for many types of clinical research, for example, studies that address causes and treatments of specific forms of psychopathology (Segal & Coolidge). Imagine a study examining different treatments for bipolar disorder. In such a study, it would be imperative to be certain that those individuals in the treatment groups actually have accurate diagnoses of bipolar disorder. Researchers must be able to accurately and definitively diagnose participants with the disorder being studied before researchers can even begin to examine theories of etiology or the effectiveness of treatment for that particular mental disorder.

In addition to increasing interrater reliability, structured interviews increase the likelihood that the diagnosis is reliable across time and across different sources of information (Rogers, 2001). In many clinical and research settings, individuals are in fact assessed on different occasions. Making multiple assessments could be dangerous if an interviewer evaluates a client in a different manner with different questions on different occasions. The client's presentation may be substantially altered because the manner in which the client is asked about those symptoms has changed instead of the client's symptoms or diagnosis being different. Using a standardized interview for multiple assessments helps ensure that if a client's presentation has changed, it is because his or her symptoms are actually different, not because of variance in interviews (Rogers). Likewise, in many settings, clinicians conduct collateral interviews with significant people in the client's life to glean a broader picture of the client's symptoms, problems, and experiences. Using a structured interview for both a client and a collateral source will likely increase the chances that discrepancies between the client and collateral informant are real, rather than a consequence of different interviewing styles (Rogers).

Advantage: Increased Validity Validity of psychiatric diagnosis refers to the meaningfulness or usefulness of the diagnosis (Coolidge & Segal, 2010b). A required prerequisite for validity is reliability. Thus, by virtue of the fact that structured interviews greatly increase reliability of diagnosis, they also increase the likelihood that the diagnosis is valid. Structured interviews also improve the validity of diagnoses in other ways. The systematic construction of structured interviews lends a methodological validity to these types of assessments compared to unstructured approaches. Because structured interviews are designed to thoroughly and accurately assess

well-defined diagnostic criteria, they are often better assessments of those criteria than unstructured interviews (Rogers, 2001). According to Rogers, clinicians who use unstructured interviews sometimes diagnose too quickly, narrow their diagnostic options too early, and miss comorbid diagnoses. Because structured interviews essentially force clinicians to assess all of the specified criteria for a broad range of diagnoses, they offer a more thorough and valid assessment of many disorders compared to unstructured interviews.

In our experience, it is common for beginning clinicians who are performing an unstructured clinical interview to gather information about the presence or absence of only a few common mental disorders. Coverage of other disorders may be neglected during an unstructured interview if the interviewer is unfamiliar with the specific criteria of some disorders. Some unstructured interviews may also provide limited information about whether comorbid psychopathology exists or about the severity of the psychopathology. Because they incorporate systematic ratings, structured and semistructured interviews easily provide information that allows for the determination of the level of severity and the level of impairment associated with a particular diagnosis. Structured interviews provide the same information about comorbid disorders as well.

Advantage: Utility as Training Tools Structured interviews can be invaluable training tools for beginning mental health professionals as well as experienced clinicians who desire to enhance their diagnostic skills. Use of structured interviews in the training context may help clinicians develop or enhance their understanding of the flow, format, and questions inherent in a comprehensive diagnostic interview. With repeated administrations, much of a structured interview can be internalized by the clinician. In addition, use of structured interviews for training may reduce anxiety, especially among neophyte clinicians, because the format and flow of the interview is laid out clearly outlined for the interviewer. This type of structure can be helpful and calming for beginning clinicians, who may be initially overwhelmed by the diagnostic process and its inherent complexity.

Structured interviews can also be a useful means of training those who make preliminary mental health assessments, for example, intake staff at hospitals, so that clients are thoroughly and accurately evaluated in preparation for treatment planning. In the case of nonclinician interviewers, fully structured interviews are advisable because they minimize the amount of clinical judgment needed for accurate administration. Use of these trained paraprofessionals can make large-scale research studies cost effective.

Disadvantage: May Hinder Rapport Despite the advantages of structured interviews, their application is not without controversy. The most common criticism of structured interviews is that their use may damage rapport or the therapeutic alliance (Segal, Maxfield, & Coolidge, 2008), which is widely viewed as an essential component of effective psychotherapy. Attaining a reliable and accurate diagnosis of a client achieves a hollow victory if the process prevents the therapeutic alliance from forming, or in a more dramatic example of clinical failure, the client does not return for continued treatment. The well-known joke poking fun at medicine, "the operation was a success but the patient died," might be recast in terms of structured

interviews as "the diagnosis was impeccable but the client never came back for another session."

How exactly might structured interviews damage rapport? Perhaps most importantly, structured interviews may impede the connection between client and clinician because interviews are problem-centered rather than person-centered. There is a danger that interviewers may get so concerned with the protocol of their interview that they fail to demonstrate the warmth, empathy, and genuine regard necessary to form a therapeutic alliance. Indeed, the standardization of the interview may play out as "routinization" (Rogers, 2003). In addition, interviewers who are overly focused on the questions that they must "get through" in an interview may, as a consequence, miss important behavioral cues or other information that could prove essential to the case.

Proponents of structured interviews note that the problem of rapport-building during a structured interview can be overcome with training, experience, and flexibility (Rogers, 2003). We concur and emphasize the observation that "rapid inquiries or monotonous questioning represents clear misuses of structured interviews" (Rogers, 2003, p. 22). If interviewers make an effort to use their basic clinical skills, structured interviews can and should be conducted in such a way that establishes rapport and enhances understanding of the client. To ensure that this is the case, however, interviewers must be aware of the potential negative effects of structured interviews on rapport-building and make the nurturance of the therapeutic alliance a prominent goal during an interview, even when they are also focused on following the protocol. It behooves those who use structured interviews to engage their respondents in a meaningful way during the interview and to avoid a rote-like interviewing style that may alienate. On the other hand, not all clients have a negative perception of a structured interview that must be intentionally overcome. Some clients actually like the structured approach to assessment because it is perceived as thorough and detailed, and in these cases, rapport is easily attained.

Disadvantage: Limited by the Validity of the Classification System Itself Earlier, we noted that proponents of structured interviews claim structured interviews may render more valid diagnoses in general. The assumption inherent in this argument is that the *DSM* diagnostic criteria are inherently valid, which is a debatable point. One should recognize that *DSM* diagnostic criteria were developed to *operationalize* theoretical constructs (e.g., depression, panic disorder, schizophrenia) so there is no absolute basis on which criteria were created. Furthermore, mental disorders are social constructions, which implies that they evolve over time as societies evolve.

Although successive editions of the *DSM* have been better grounded in empirical research, and the criteria for some disorders (e.g., major depression) have solid research support, other disorders (e.g., most of the personality disorders) and their criteria have not been examined as consistently or as completely, therefore leaving questions about their validity (Widiger & Trull, 2007). This point is also bolstered by the fact that the criteria for some disorders have changed significantly from one edition to another in the evolution of the *DSM* (Coolidge & Segal, 1998; Segal, 2010). Furthermore, criteria for many disorders in the *DSM* are impacted by cultural and subcultural variations in the respondent (see Chapter 4 in this book), as well as by the age of the respondent. Indeed, the diagnostic criteria for many mental disorders do not

fit the context of later life and, therefore, some criteria do not adequately capture the presentation of the disorders among many older adults (e.g., Segal, Coolidge, & Rosowsky, 2006; Segal, Qualls, & Smyer, 2011). Thus, certain criteria may be valid only for a particular group of individuals, at a particular point in time, at a particular age. The primary method clinicians currently use to conceptualize diagnoses (the *DSM*), while improving, is far from perfect. Because the *DSM* generally does poorly in attending to these issues of age and diversity, interviews based on poor-fitting diagnostic criteria are similarly limited.

In addition to potential problems with *DSM* diagnostic criteria, another issue regarding structured interviews is that it is challenging to establish firmly the validity of any particular structured interview. The quandary is that our best means of establishing the validity of a structured interview is to compare diagnoses obtained from such interviews to diagnoses obtained by expert clinicians or by other structured interviews. This is inherently problematic because we cannot be certain that diagnoses by experts or other structured interviews are in fact valid in the first place (Segal et al., 2008).

Disadvantage: The Trade-Off of Breadth Versus Depth A final criticism of structured interviews centers on the fact that no one structured interview can be all things in all situations, covering all disorders and eventualities. For example, if a structured interview has been designed to cover an entire diagnostic system (like the *DSM*, which identifies several hundred specific mental disorders), then inquiries about each disorder must be limited to a few inclusion criteria. In this case, the fidelity of the official diagnostic criteria has been compromised for the sake of a comprehensive interview. If the fidelity of the criteria is not compromised, then the structured interview becomes unwieldy in terms of time and effort required for its full administration. Most structured interviews attempt some kind of compromise between these two points of tension.

Thus, regarding breadth versus depth of approach, users of structured interviews are forced to make a choice about what is most useful in a given situation. Both choices have their limitations. If clinicians or researchers decide to use an interview that provides great breadth of information, they ensure that a wide range of disorders and a great many different areas of a respondent's life are assessed. However, one may not have the depth of information needed to fully conceptualize a case. On the other hand, deciding to use an interview focused on a few specific areas will provide clinicians and researchers with a wealth of information about those specific areas, but it may result in missing information that could lead to additional diagnoses or a different case conceptualization. Thus, it is essential to understand that when choosing a particular structured or semistructured interview, there are often tradeoffs regarding breadth and depth of information.

Weighing Advantages and Disadvantages

Our examination of the strengths and limitations of structured interviews highlights the importance of carefully contemplating what is needed in a particular clinical or research situation before choosing a structured interview. Structured interviews can be invaluable tools in both clinical and research work; however, it is essential that one does not use such tools without accounting for some of the problems inherent in their

use. Rogers (2001) voiced the helpful perspective that it would be unwise to view the interviewing process as an either/or proposition (i.e., unstructured vs. structured interview). In certain situations, unstructured interviews may meet the objectives of a particular clinical inquiry more efficiently than a structured interview. For example, in a crisis situation, flexibility on the part of the clinician is required to meet the pressing demands of this fluid and potentially volatile interaction. However, in other cases, greater assurances that the diagnostic conclusions are valid and meaningful would take priority, for example, in clinical research or in the delivery of clearly defined psychotherapeutic intervention protocols. As noted earlier, the integration of a nonstandardized or clinical interview with a structured or semistructured interview may also be an excellent option for clinicians and researchers.

Finally, despite some potential limitations to the use of structured and semistructured interviews, their use has clearly revolutionized the diagnostic process, vastly improving diagnostic reliability and validity. Such interviews have greatly improved clinical and research endeavors by providing a more standardized, scientific, and quantitative approach to the evaluation of specific symptoms and mental disorders. As such, it is likely that the use of structured and semistructured interviews will increase in the coming decades.

STRUCTURED AND SEMISTRUCTURED INTERVIEWS FOR DIFFERENTIAL DIAGNOSIS

In this section, we examine several popular structured and semistructured interviews. These interviews can be divided into those that focus on either clinical disorders or personality disorders. As noted earlier, although the *DSM-5* no longer makes a distinction between clinical disorders and personality disorders (with the replacement of the multiaxial coding system with a nonaxial coding system), the distinction is still relevant to the current crop of structured and semistructured interviews that were developed with this difference in mind. Instruments that focus on clinical disorders include the Anxiety Disorders Interview Schedule for *DSM-IV*, Diagnostic Interview Schedule for *DSM-IV*, the Schedule for Affective Disorders and Schizophrenia, and the Structured Clinical Interview for *DSM-IV* Axis I Disorders. Instruments that measure personality disorders include the Diagnostic Interview for *DSM* Personality Disorders, the International Personality Disorder Examination, the Structured Clinical Interview for *DSM-IV* Axis II Personality Disorders, and the Structured Interview for *DSM-IV* Personality.

Where possible, we describe forthcoming updates to some of these instruments as they are revised to conform to the current *DSM-5* system. A general overview of each instrument is provided in Table 3.2. Each instrument assesses a variety of mental disorders and, therefore, can assist in the important task of differential diagnosis (i.e., a systematic way of discriminating among numerous possible disorders to identify specific ones for which the client meets the diagnostic threshold). Each interview also allows for an assessment of many comorbid mental disorders. The instruments presented in this chapter do not represent an exhaustive list of structured and semistructured interviews, but they are among the most common and well-validated ones. Interested readers are referred to Rogers (2001) and Summerfeldt, Kloosterman, and Antony (2010) for coverage of instruments not reviewed in this chapter.

Table 3.2
Comparison of Major Diagnostic Interviews

Name	Time Required	Format	Comment
Anxiety Disorders Interview Schedule for DSM-IV (Brown, DiNardo, & Barlow, 1994a)	45 to 60 minutes	Semistructured, interviewer administered	Provides in-depth assessment of anxiety disorders and other frequently comorbid conditions (e.g., mood disorders, substance abuse). Designed to be administered by trained mental health professionals with training in administration. Available in separate current and lifetime versions.
Diagnostic Interview Schedule for *DSM-IV* (Robins et al., 2000)	90 to 150 minutes	Fully structured, computerized, closed-ended questions	Designed for epidemiological research. Includes all possible diagnoses in *DSM-IV*. Can be administered by nonclinicians, although interviewers must receive specialized training.
Schedule for Affective Disorders and Schizophrenia (Endicott & Spitzer, 1978)	90 to 150 minutes	Semistructured, interviewer administered	Provides in-depth coverage on clinical disorders, namely mood and psychotic disorders. Designed for administration by trained mental health professionals, and additional training in administration is required.
Structured Clinical Interview for *DSM-IV* Axis I Disorders (First, Spitzer, Gibbon, & Williams, 1997a)	45 to 90 minutes	Semistructured, interviewer administered	Covers *DSM-IV* clinical disorders most commonly seen in clinical settings. Designed for use by professionals with knowledge of psychopathology, *DSM-IV* diagnostic criteria, and basic interviewing skills. Research Version and Clinical Version available.
Diagnostic Interview for *DSM-IV* Personality Disorders (Zanarini, Frankenburg, Sickel, & Yong, 1996)	90 minutes	Semistructured, interviewer administered	Designed to assess the 10 standard *DSM-IV* personality disorders. Requirements for administration include at minimum a bachelor's degree, at least 1 year of clinical experience with personality-disordered clients, and several training interviews.

International Personality Disorder Examination (Loranger, 1999)	15 minutes (self-administered screen), 90 minutes (interview)	Contains self-administered pencil-and-paper questionnaire and semistructured interview	Evaluates personality disorders for both the *DSM-IV* and the *International Classification of Diseases*, 10th ed. (*ICD-10*). Intended for use by experienced clinicians with specialized training in administration.
Structured Clinical Interview for *DSM-IV* Axis II Personality Disorders (First, Gibbon, Spitzer, Williams, & Benjamin, 1997)	20 minutes (self-administered screen), 60 minutes (interview)	Contains self-report screening questionnaire and semistructured interview	Assesses the 10 standard *DSM-IV* personality disorders. Designed for administration by professionals with knowledge of psychopathology, *DSM-IV* diagnostic criteria, and basic interviewing skills.
Structured Interview for *DSM-IV* Personality (Pfohl, Blum, & Zimmerman, 1997)	60 to 90 minutes	Semistructured interview	Comprehensive interview for *DSM-IV* personality disorders. Collateral sources encouraged. Requirements for administration include an undergraduate degree in the social sciences and 6 months' experience with diagnostic interviewing in addition to specialized training.

Structured and Semistructured Interviews for Clinical Disorders

Anxiety Disorders Interview Schedule for DSM-IV The Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV; Brown, DiNardo, & Barlow, 1994a) is a semistructured clinician-administered interview designed to measure current episodes of anxiety disorders as defined by the *DSM-IV*. It provides differential diagnosis among anxiety disorders and includes sections on mood, somatoform, and substance use disorders, as anxiety disorders are frequently comorbid with such conditions. There are two versions of the adult ADIS-IV: the Standard Version, which provides only current diagnostic information, and the Lifetime Version (ADIS-IV-L; DiNardo, Brown, & Barlow, 1994), which offers both past and current diagnostic information. The ADIS-IV-L is similar in structure to the ADIS-IV, but contains separate sections that assess the occurrence of disorders in the past. The ADIS-IV can be used in both clinical and research settings.

At the beginning of the ADIS-IV, basic demographic information is collected as well as a short description of the presenting problem. This information gives the examiner an idea of which topics should be pursued in more detail throughout the interview. Following the presenting problem, the examiner asks the respondent, "What would you say is the main reason that brought you here today?" and the response is recorded verbatim. Next, the respondent is asked to describe any recent struggles in functioning within the past year (e.g., school, work, relationships). The interview then continues

with the assessment of anxiety disorders. This section begins with the more prevalent anxiety disorders (e.g., panic disorder, agoraphobia, social phobia) and is organized logically to reflect the shared symptoms among many anxiety disorders. Subsequent to this segment are sections assessing mood disorders, somatoform disorders, mixed anxiety/depression disorders, alcohol and substance use/dependence, and psychotic and conversion symptoms. A segment assessing the individual's family history of psychological disorders is also included. At the end of the ADIS-IV, the examiner administers the Hamilton Rating Scale for Depression and the Hamilton Anxiety Rating Scale. The clinician manual (Brown, DiNardo, & Barlow, 1994b) notes that these scales are useful as they provide a general assessment of current depressive and anxious symptoms.

Each section on the ADIS-IV includes items assessing diagnostic criteria for the given disorder. The examiner begins with several dichotomous yes/no initial inquiry questions, and answers of "yes" warrant asking more extensive questions to gauge the presence or absence of the particular disorder. In some sections, these dichotomous items are considered skip-out points in which, pending negative ratings, continuation is not necessary. Dimensional ratings are also obtained regarding both current and past experiences of major symptoms of the given disorder. As noted previously, the ADIS-IV-L contains separate sections for current and past occurrences of disorders, whereas the ADIS-IV assesses only current disorders. However, the ADIS-IV contains screening questions for past episodes in the initial inquiry items. If the respondent denotes a positive response to these particular screening questions, the clinician's manual recommends that the interviewer adapt other items in that section to obtain information about previous disorders. The manual notes that this information may be useful in differential diagnosis.

After the initial inquiry section, the clinician continues with the current episode segment of the interview, which provides items that collectively assess all diagnostic criteria for a particular disorder. The questions in the current episode section are arranged so that they begin as open-ended and are followed by more specific inquiries. The need for the more specific inquiries is contingent upon the response to the initial open-ended question. For instance, if the respondent provides a specific response to a question regarding the timeline of a given symptom (e.g., "The symptom began around one month ago"), then follow-up questions may not be needed. The current episode section also contains questions that assess the onset of the disorder and etiological factors. At the conclusion of the current episode section, the administrator again inquires about past episodes of the disorder. The purpose of this repeated item is that the interviewer can reassess the previous occurrence of the disorder given the wealth of diagnostic information collected in that section. In the ADIS-IV-L, the current episode portion of the interview is followed by the past episode section, which is similar in structure to the current episode segment.

The ADIS-IV contains a score sheet in which the interviewer records diagnoses (including dates of onset) in addition to a diagnostic confidence rating (0–100, 100 indicating complete certainty). If the diagnostic confidence rating is less than 100, the interviewer must indicate why. Each disorder listed is given a rating of clinical severity ranging from 0 to 8, with higher numbers indicating more distress. Ratings of 0 indicate that there are no features of a given disorder present. These ratings are used to identify clinical versus subclinical disorders, such that ratings of 3 or below indicate

subsyndromal symptomatology, and ratings of 4 and above indicate the presence of a disorder (as per the *DSM-IV* criteria). The ADIS-IV-L also contains a "diagnostic timeline" page that synthesizes information regarding the temporal sequence of disorders as well as etiology.

The ADIS-IV is designed for use by experienced clinicians who are familiar with the *DSM-IV* as well as the ADIS-IV. Examiners are encouraged to use clinical judgment to determine whether an item should be read verbatim or re-worded as needed (e.g., shortening length and complexity of questions for those with lower levels of education). Examiners are also encouraged to use their clinical judgment to gather further clarifying information from respondents, and to decide when to skip certain sections of the interview.

Overall, both the ADIS-IV and ADIS-IV-L are popular and valuable tools in diagnosing anxiety disorders as well as frequently comorbid conditions. Studies have indicated empirical support regarding the reliability and validity of the ADIS-IV and ADIS-IV-L, and interested readers are referred to Grisham, Brown, and Campbell (2004) for a summary of the psychometric properties of both instruments. The ADIS-IV and ADIS-IV-L have been translated into at least five other languages, and they also have been adapted into a version for use with children.

The ADIS was recently significantly updated to match changes in *DSM-5*. The interview name changed slightly, and is called the Anxiety and Related Disorders Interview Schedule for *DSM-5* (ADIS-5; Brown & Barlow, 2014a). A lifetime version of the ADIS-5 is also available (Brown & Barlow, 2014b). The ADIS-5 interview and manual are available from Oxford University Press (www.us.oup.com).

Diagnostic Interview Schedule for DSM-IV The Diagnostic Interview Schedule for *DSM-IV* (DIS-IV; Robins et al., 2000) is designed to ascertain the presence or absence of major mental disorders of the *DSM-IV* (APA, 1994). It is unique among the multidisorder diagnostic interviews in that it is a *fully structured* interview specifically designed for use by nonclinician interviewers, whereas the other interviews are semistructured. By definition, a fully structured interview clearly specifies all questions and probes and does not permit deviations.

The original DIS was developed in 1978 at the request of the National Institute of Mental Health Division of Biometry and Epidemiology, which was commencing a series of large-scale, multicenter epidemiological investigations of mental disorders in the general adult population in the United States. The development of a structured interview that could be administered by nonclinicians was imperative because of the prohibitive cost of using professional clinicians as interviewers. As a result, the DIS was designed as a fully structured diagnostic interview explicitly crafted so that it could be administered and scored by nonclinician interviewers.

To ensure standardized administration of the DIS-IV, computerized administration is required, which may be administered by the interviewer or it may be self-administered. In both formats, the exact wording of all questions and probes is presented to the respondent in a fixed order on a computer screen. Rephrasing of questions is discouraged, although DIS-IV interviewers can repeat questions as necessary to ensure that the respondent understands them. All questions are closed-ended, and replies are coded with a forced-choice yes-or-no response format. The DIS-IV gathers all necessary information about the person from his or her

self-report. Collateral sources of information are not used. The DIS-IV is self-contained and covers all necessary symptoms to make many *DSM-IV* diagnoses. To this end, the *DSM-IV* diagnostic criteria for the disorders have been faithfully turned into specific questions on the DIS-IV. The coded responses are directly entered into a database during the interview, and the diagnosis is made according to the explicit rules of the *DSM-IV* diagnostic system.

Because the DIS-IV was designed for epidemiological research with normative samples, interviewers do not elicit a presenting problem from the respondent, as would be typical in unstructured clinical interviews. Rather, interviewers begin by asking questions about symptoms in a standardized order. Like most of the other structured interviews examined here, the DIS-IV has sections that cover different disorders. Each diagnostic section is independent, except where one diagnosis preempts another. Once a symptom is reported to be present, further closed-ended questions are asked about diagnostically relevant information, such as severity, frequency, time frame, and possibility of organic etiology of the symptom. The DIS-IV includes a set of core questions that are asked of each respondent. Core questions are followed by contingent questions that are administered only if the preceding core question is endorsed. Interviewers use a probe flowchart that indicates which probes to select in which circumstances.

For each symptom, the respondent is asked to state whether it has ever been present and how recently. All data about the presence or absence of symptoms and time frames of occurrence are coded and entered into the computer. Consistent with its use of nonclinician interviewers who may not be overly familiar with the *DSM-IV* or psychiatric diagnosis, the diagnostic output of the DIS-IV is generated by a computer program that analyzes data from the completed interview. The output provides estimates of prevalence for two time periods: current and lifetime.

Due to its highly structured format, full administration of the DIS-IV typically requires between 90 and 150 minutes. To shorten administration time, the modular format makes it possible to drop evaluation of disorders that are not of interest in a particular study. Another option is to drop further questioning for a particular disorder once it is clear that the threshold number of symptoms needed for diagnosis will not be met. Although designed for use by nonclinician administrators, training for competent administration of the DIS-IV is necessary. Trainees typically attend a 1-week training program at Washington University (St. Louis, Missouri), during which they review the DIS-IV manual, listen to didactic presentations about the structure and conventions of the DIS-IV, view recorded vignettes, complete workbook exercises, and conduct several practice interviews followed by feedback and review. Additional supervised practice is also recommended.

The psychometric properties of the original DIS and its revisions are excellent, and such data has been documented in an impressive array of studies. Interested readers are referred to Compton and Cottler (2004) for an excellent summary of the psychometric characteristics of the DIS-IV. Overall, the DIS-IV has proven to be a popular and useful diagnostic assessment tool, especially for large-scale epidemiological research. The DIS-IV has been translated into more than a dozen languages, is used in countries across the globe for epidemiological research, and served as the basis for the Composite International Diagnostic Interview used by the World Health Organization. The lead authors of the DIS are working on updating the DIS-IV to include

changes reflected in the *DSM-5*. It is anticipated that the updated modules will follow the criteria for new diagnoses and will offer a more streamlined probe flowchart (L. Cottler, personal communication, July 20, 2013). For further information on DIS-IV materials, training, and developments, refer to the DIS website (http://epi.wustl.edu).

Schedule for Affective Disorders and Schizophrenia The Schedule for Affective Disorders and Schizophrenia (SADS; Endicott & Spitzer, 1978) is a semistructured diagnostic interview designed to evaluate a range of clinical disorders, with a focus on mood and psychotic disorders. Ancillary coverage is provided for anxiety symptoms, substance abuse, psychosocial treatment history, and antisocial personality features. The SADS provides in-depth but focused coverage of the mood and psychotic disorders and also supplies meaningful distinctions of impairment in the clinical range for these disorders. The SADS can be used to make many *DSM-IV* diagnoses, but it is not completely aligned with the *DSM* system representing a significant point of concern. With substantive changes made in *DSM-5*, the SADS is at risk for becoming more outdated if it is not revised substantially.

The SADS is intended to be administered to adult respondents by trained mental health professionals. It focuses heavily on the differential diagnosis of mood and psychotic disorders, with great depth of assessment in these areas. In the beginning of the interview, a brief overview of the respondent's background and psychiatric problems is elicited in an open-ended inquiry. The SADS is then divided into two parts, each focusing on a different time period. Part I provides for a thorough evaluation of current psychiatric problems and concomitant functional impairment. A unique feature of the SADS is that, for the current episode, symptoms are rated when they were at their worst levels to increase diagnostic sensitivity and validity. In contrast, Part II provides a broad overview of past episodes of psychopathology and treatment. Overall, the SADS covers more than 20 diagnoses in a systematic and comprehensive fashion and provides for diagnosis of both current and lifetime psychiatric disorders. Some examples include schizophrenia (with 6 subtypes), schizoaffective disorder, manic disorder, hypomanic disorder, major depressive disorder (with 11 subtypes), minor depressive disorder, panic disorder, obsessive-compulsive disorder, phobic disorder, alcoholism, and antisocial personality disorder (Endicott & Spitzer, 1978). In *DSM-5*, the subtypes of schizophrenia have been deleted (due to poor validity and clinical utility) so the distinction made by the SADS in this area may not be of much use in the future.

In the SADS, questions are clustered according to specific diagnoses. For each disorder, standard questions are specified to evaluate specific symptoms of that disorder. Questions are either dichotomous or rated on a Likert-type scale, which allows for uniform documentation of levels of severity, persistence, and functional impairment associated with each symptom. To supplement client self-report and obtain the most accurate symptom picture, the SADS allows for consideration of all available sources of information (i.e., chart records, input from relatives). In addition to the standard questions asked of each respondent, optional probes may be selectively used to clarify responses, and unstructured questions may be generated by the interviewer to augment answers to the optional probes. Thus, considerable clinical experience and judgment are needed to administer the SADS. To reduce length of administration and evaluation of symptoms that are not diagnostically significant,

many diagnostic sections begin with screening questions that provide for skip-outs to the next section if the respondent shows no evidence of having the disorder. Administration of the SADS typically takes between 90 and 150 minutes. The interviewer makes formal diagnostic appraisals after the interview is completed. No computer scoring applications have been designed for the SADS because of the complex nature of the diagnostic process and the strong reliance on clinical judgment.

As noted earlier, the SADS was designed for use by trained clinicians. Considerable clinical judgment, interviewing skills, and familiarity with diagnostic criteria and psychiatric symptoms are requisite for competent administration. As such, it is recommended that the SADS only be administered by professionals with graduate degrees and clinical experience, such as clinical psychologists, psychiatrists, and psychiatric social workers (Endicott & Spitzer, 1978). Training in the SADS is intensive and can encompass several weeks. The process includes reviewing the most recent SADS manual and practice in rating written case vignettes and videotaped SADS interviews. Additionally, trainees typically watch and score live interviews as if participating in a reliability study with a simultaneous-rating design. Throughout, discussion and clarification with expert interviewers regarding diagnostic disagreements or difficulties add to the experience. Finally, trainees conduct their own SADS interviews that are observed and critiqued by the expert trainers.

Numerous additional versions of the SADS have been devised, each with a distinct focus and purpose. Perhaps the most common is the SADS-L (Lifetime version), which can be used to make both current and lifetime diagnoses but has significantly fewer details about current psychopathology than the full SADS and results in a quicker administration time. The SADS-L generally is used with nonpsychiatric samples in which there is no assumption of a significant current psychiatric problem. The SADS-Change Version is also popular and consists of 45 key symptoms from the SADS Part 1. Extensive study of the SADS suggests that it possesses excellent psychometric characteristics. See Rogers, Jackson, and Cashel (2004) for a comprehensive review of these data.

The SADS has been translated into several languages, but its primary use has been in North America. The SADS has been widely used in clinical research over the past three decades, and consequently has a large body of empirical data associated with it. As such, it is often the instrument of choice for clinical researchers desiring in-depth assessment of depression and schizophrenia. The extensive subtyping of disorders provided by the SADS is also highly valued by clinical researchers. However, owing to its length and complexity, the SADS is infrequently chosen for use in many traditional, pure clinical settings (e.g., community mental health centers). Because the SADS is most closely aligned with the Research Diagnostic Criteria (and not the *DSM* criteria), there are no plans to update the measure to fit the *DSM-5* (J. Endicott, personal communication, July 17, 2013).

Structured Clinical Interview for DSM-IV Axis I Disorders The Structured Clinical Interview for *DSM-IV* Axis I Disorders (SCID-I) is a flexible, semistructured diagnostic interview designed for use by trained clinicians to diagnose many adult *DSM-IV* clinical disorders. The SCID-I has widespread popularity as an instrument to obtain reliable and valid psychiatric diagnoses for clinical, research, and training purposes, and it has been used in more than 1,000 studies.

The original SCID was designed for application in both research and clinical settings. Recently, the SCID has been split into two distinct versions: the Research Version and the Clinician Version. The Research Version covers more disorders, subtypes, and course specifiers than the Clinician Version and, therefore, takes longer to complete. The benefit, however, is that it provides for a wealth of diagnostic data that is particularly valued by clinical researchers. The research version is distributed by the Biometrics Research Department of the New York State Psychiatric Institute (http://nyspi.org).

The Clinician Version of the SCID (SCID-CV; First, Spitzer, Gibbon, & Williams, 1997a) is designed for use in clinical settings. It has been trimmed to encompass only those *DSM-IV* disorders that are most typically seen in clinical practice and can further be abbreviated on a module-by-module basis. The SCID-CV contains six self-contained modules of major diagnostic categories (Mood Episodes, Psychotic Symptoms, Psychotic Disorders, Mood Disorders, Substance Use Disorders, and Anxiety and Other Disorders).

The modular design of the SCID represents a major strength of the instrument, because administration can be customized easily to meet the unique needs of the user. For example, the SCID can be shortened or lengthened to include only those categories of interest, and the order of modules can be altered. The format and sequence of the SCID was designed to approximate the flowcharts and decision trees followed by experienced diagnostic interviewers. The SCID begins with an open-ended overview portion, during which the development and history of the present psychological disturbance are elicited and tentative diagnostic hypotheses are generated. Then, the SCID systematically presents modules that allow for assessment of specific disorders and symptoms. Most disorders are evaluated for two time periods: current (meets criteria for the past month) and lifetime (ever-met criteria).

Consistent with its linkage with *DSM-IV*, formal diagnostic criteria are included in the SCID booklet, thus permitting interviewers to see the exact criteria to which the SCID questions pertain. This unique feature makes the SCID an outstanding training tool for clinicians because it facilitates the learning of diagnostic criteria and presents excellent questions to assess the criteria. The SCID has many open-ended prompts that encourage respondents to elaborate freely about their symptoms. At times, open-ended prompts are followed by closed-ended questions to clarify fully a particular symptom. Although the SCID provides structure to cover criteria for each disorder, its semistructured format provides significant latitude for interviewers to restate questions, ask for further clarification, probe, and challenge if the initial prompt was misunderstood by the interviewee or clarification is needed to rate a symptom. SCID interviewers are encouraged to use all sources of information about a respondent, and gentle challenging of the respondent is encouraged if discrepant information is suspected.

During administration, each symptom is rated as either absent (or below threshold) or present (and clinically significant). A question mark (?) denotes that inadequate information was obtained to code the symptom. The SCID flowchart instructs interviewers to skip out of a particular diagnostic section when essential symptoms are judged to be below threshold or absent. These skip-outs result in decreased time of administration as well as the skipping of items with no diagnostic significance. Administration of the SCID is typically completed in one session and takes from

45 to 90 minutes. Once administration is completed, all current and past disorders for which criteria are met are listed on a Diagnostic Summary sheet.

The SCID is optimally administered by trained clinicians. Because of the semi-structured format of the SCID, proper administration often requires that interviewers restate or clarify questions in ways that are sometimes not clearly outlined in the manual to judge accurately if a particular diagnostic criterion has been met. The task requires that SCID assessors have a working knowledge of psychopathology, *DSM-IV* diagnostic criteria, and basic interviewing skills. Standard procedures for training to use the SCID include carefully reading the *Users Guide to the SCID* (First, Spitzer, Gibbon, & Williams, 1997b), reviewing the SCID administration booklet and score sheet, viewing SCID videotape training materials that are available from the SCID authors, and conducting role-played practice administrations with extensive feedback discussions. Next, trainees may administer the SCID to representative participants who are jointly rated so that a discussion about sources of disagreements can ensue. In research settings, a formal reliability study is advantageous. The reliability and validity of the SCID in adult populations with diverse disorders has been evaluated in several investigations, with generally excellent results among widely varied participant samples and experimental designs (see review by First & Gibbon, 2004; Segal, Hersen & Van Hasselt, 1994).

Overall, the SCID is a widely used and respected assessment instrument. It has been translated into 12 languages and has been applied successfully in research studies and clinical practice in many countries. Computer-assisted clinician-administered versions of the SCID-CV and SCID Research Version are available. A self-administered computerized screening version of the SCID, called the SCID-Screen-PQ, is also available, but it does not produce final diagnoses. Rather, likely diagnoses are further evaluated by a full SCID interview or a clinical evaluation.

The SCID is currently being modified to reflect changes in the *DSM-5*. The new measure will be called the Structured Clinical Interview for *DSM-5* Disorders. Developers of the instrument are adding several new disorders including hoarding, premenstrual dysphoric disorder, trichotillomania, excoriation (skin picking) disorder, intermittent explosive disorder, gambling disorder, and attention-deficit/hyperactivity disorder (M. First, personal communication, May 9, 2013). In addition, screening for substance abuse will occur prior to the diagnostic modules of the SCID so that the effects of the client's substance use can be clarified from the beginning of the interview. For more information on the SCID, visit the SCID website (www.scid4.org).

Semistructured Interviews for Personality Disorders

Diagnostic Interview for Personality Disorders The Diagnostic Interview for *DSM-IV* Personality Disorders (DIPD-IV; Zanarini, Frankenburg, Sickel, & Yong, 1996) is a semistructured interview designed to assess the presence or absence of the 10 standard *DSM-IV* personality disorders as well as depressive personality disorder and passive-aggressive personality disorder in the *DSM-IV* appendix. Prior to personality disorder assessment, a full screening for clinical disorders is recommended. Additionally, an assessment of the respondent's general functioning (e.g., in the domains of work, school, and social life) is advised before administration of the DIPD-IV (Zanarini et al., 1996).

The interview is conducted on a disorder-by-disorder basis. The interview contains 108 sets of questions, each designed to assess a specific *DSM-IV* personality disorder diagnostic criterion. The *DSM-IV* criterion is provided in bold below each set of questions for easy cross-reference. The initial question for each criterion typically has a yes-no format that is followed by open-ended questions to explore more fully clients' experiences. Clients are informed that the interview pertains to the past 2 years of their life and that the interviewer wants to learn about the thoughts, feelings, and behaviors that have been typical for them during the 2-year period. Whereas clients are the sole source of information for rating most of the diagnostic criteria, behavior exhibited during the interview is valued and may override client self-report if there are contradictions. The administrator is encouraged to probe further if responses appear incomplete or fallacious.

Each diagnostic criterion is rated on the following scale: 0 indicates absent or clinically insignificant, 1 indicates present but of uncertain clinical significance, 2 indicates present and clinically significant, and NA indicates not applicable. After all 108 criteria are evaluated, final categorical diagnosis for each personality disorder is made based on the number of criteria met. The final output is recorded as 2, indicating yes or met full criteria, 1 indicating subthreshold (one less than required number of criteria), or 0 indicating no.

Information about administration and scoring of the DIPD-IV is relatively sparse, at least compared to the other interviews focusing on personality disorders. The training requirements include at minimum a bachelor's degree, at least one year of clinical experience with personality-disordered clients, and several training interviews in which the person observes skilled administrators and then administers the interview. Training tapes and workshops are available, as is a Spanish version. Administration time is typically about 90 minutes. Most notably, the DIPD-IV has been chosen as the primary diagnostic measure for personality disorders in the Collaborative Longitudinal Personality Disorders Study, which is a large, multisite, prospective naturalistic longitudinal study of personality disorders and comorbid mental health problems. Because personality disorder criteria have not changed in the *DSM-5* there will be no changes to the DIPD-IV (M.C. Zanarini, personal communication, July 18, 2013). For further information on the DIPD-IV, contact Dr. Mary C. Zanarini (zanarini@mclean.harvard.edu).

International Personality Disorder Examination The International Personality Disorder Examination (IPDE; Loranger, 1999) is an extensive, semistructured diagnostic interview administered by experienced clinicians to evaluate personality disorders for both the *DSM-IV* and the *International Classification of Diseases,* 10th ed. (*ICD-10*) classification systems. The IPDE was developed within the Joint Program for the Diagnosis and Classification of Mental Disorders of the World Health Organization and U.S. National Institutes of Health aimed at producing a standardized assessment instrument to measure personality disorders on a worldwide basis. As such, the IPDE is the only personality disorder interview based on worldwide field trials. The IPDE manual contains the interview questions to assess either the 11 *DSM-IV* or the 10 *ICD-10* personality disorders. The two IPDE modules (*DSM-IV* and *ICD-10*) contain both a self-administered screening questionnaire and a semistructured interview booklet with scoring materials.

The Screening Questionnaire is a self-administered form that contains 77 *DSM-IV* or 59 *ICD-10* items written at a fourth-grade reading level. Items are answered either "true" or "false," and the questionnaire is typically completed in about 15 minutes. The clinician can quickly score the questionnaire and identify those respondents whose scores suggest the presence of a personality disorder. Subsequently, the IPDE clinical interview is administered.

The IPDE Interview modules (for either the *DSM-IV* or *ICD-10* systems) contain questions, each reflecting a personality disorder criterion, that are grouped into six thematic headings: work, self, interpersonal relationships, affects, reality testing, and impulse control (Loranger, 1999). Because disorders are not covered on a one-by-one basis, the intent of the evaluation is less transparent, similar to the SIDP-IV. At the beginning of each section, open-ended inquiries are provided to enable a smooth transition from the previous section and to encourage respondents to elaborate about themselves in a less structured fashion. Then, specific questions are asked to evaluate each personality disorder criterion. For each question, the corresponding personality disorder and the specific diagnostic criterion are identified with specific scoring guidelines.

Respondents are encouraged to report their typical or usual functioning, rather than their personality functioning during times of episodic psychiatric disturbance. The IPDE requires that a trait be prominent during the past 5 years to be considered a part of the respondent's personality. Information about age of onset of particular behaviors is explored to determine if a late-onset diagnosis (after age 25 years) is appropriate. When a respondent acknowledges a particular trait, interviewers follow up by asking for examples and anecdotes to clarify the trait or behavior, gauge the impact of the trait on the person's functioning, and fully substantiate the rating. Such probing requires significant clinical judgment and knowledge on the part of interviewers about each criterion. Items may also be rated based on observation of the respondent's behavior during the session, and this too requires a certain level of clinical expertise. To supplement self-report, an interview of informants is encouraged. Clinical judgment is needed to ascertain which source is more reliable if inconsistencies arise.

Each criterion is rated on a scale with the following definitions: 0 indicates that the behavior or trait is absent or within normal limits, 1 refers to exaggerated or accentuated degree of the trait, 2 signifies criterion level or pathological, and ? indicates the respondent refuses or is unable to answer. Comprehensive item-by-item scoring guidelines are provided in the manual (Loranger, 1999). At the end of the interview, the clinician records the scores for each response on the appropriate IPDE Answer Sheet. Ratings are then collated either by hand or computer. The ultimate output is extensive, including presence or absence of each criterion, number of criteria met for each personality disorder, a dimensional score (sum of individual scores for each criterion for each disorder), and a categorical diagnosis (definite, probable, or negative) for each personality disorder (Loranger, 1999). Such comprehensive output is often of value to clinical researchers.

The IPDE is intended to be administered by experienced clinicians who have also received specific training in the use of the IPDE. Such training typically involves a workshop with demonstration videotapes, discussions, and practice. Average administration time is 90 minutes for the interview, which can be reduced by using the screening questionnaire (omitting interview items associated with unlikely

personality disorders). Because the IPDE has been selected by the WHO for international application, it has been translated into numerous languages to facilitate cross-cultural research. Ample evidence of reliability and validity of the IPDE has been documented (Loranger, 1999; Loranger et al., 1994). Because of the instrument's ties to the *DSM-IV* and *ICD-10* classification systems and adoption by the WHO, the IPDE is widely used for international and cross-cultural investigations of personality disorders. No major updates to the IPDE are planned at present.

Structured Clinical Interview for DSM-IV Axis II Personality Disorders To complement the clinical disorder I version of the SCID, a version focusing on personality disorders according to *DSM-IV* has been developed, and it is called the Structured Clinical Interview for *DSM-IV* Axis II Personality Disorders (SCID-II; First, Gibbon, Spitzer, Williams, & Benjamin, 1997). The SCID-II has a similar semistructured format as the original SCID but it covers the 10 standard *DSM-IV* personality disorders, as well as depressive personality disorder and passive-aggressive personality disorder (which were listed as disorders to be studied further in an appendix of the *DSM-IV*).

For comprehensive assessment, the SCID-II may be easily used in conjunction with the original SCID that would be administered prior to personality disorder assessment. This is encouraged so that the respondent's present mental state can be considered when judging accuracy of self-reported personality traits. The basic structure and conventions of the SCID-II closely resemble those of the SCID-I. An additional feature of the SCID-II is that it includes a 119-item self-report screening component called the Personality Questionnaire that may be administered prior to the interview portion and takes about 20 minutes. The purpose of the Personality Questionnaire is to reduce overall administration time, because only those items that are scored in the pathological direction are further evaluated during the structured interview portion.

During the structured interview component, the pathologically endorsed screening responses are further pursued to determine whether the symptoms are actually experienced at clinically significant levels. Here, the respondent is asked to elaborate about each suspected personality disorder criteria and specified prompts are provided. Like the original SCID, the *DSM-IV* diagnostic criteria are printed on the interview page for easy review, and responses are coded as follows: ? indicates inadequate information, 1 indicates absent or false, 2 indicates subthreshold, and 3 indicates threshold or true. Each personality disorder is assessed completely, and diagnoses are completed before proceeding to the next disorder. The modular format permits researchers and clinicians to tailor the SCID-II to their specific needs and reduce administration time. Clinicians who administer the SCID-II are expected to use their clinical judgment to clarify responses, gently challenge inconsistencies, and ask for additional information as required to rate accurately each criterion. Collection of diagnostic information from ancillary sources is permitted. Complete administration of the SCID-II typically takes less than 60 minutes.

Training requirements and interviewer qualifications are similar to that of the original SCID. There is no Clinician Version of the SCID-II. The psychometric properties of the SCID-II are strong (see comprehensive review by First and Gibbon, 2004). Given the extensive coverage of the personality disorders, modular approach, and strong operating characteristics, the SCID-II should remain a popular and

effective tool for personality disorder assessment. To be consistent with the removal of the multiaxial system in the *DSM-5*, the SCID-II will be renamed the SCID-Personality Disorders (SCID-PD) but no other changes are imminent. The SCID-II website is the same as for the original SCID (www.scid4.org).

Structured Interview for DSM-IV Personality The Structured Interview for *DSM-IV* Personality (SIDP-IV; Pfohl, Blum, & Zimmerman, 1997) is a comprehensive semi-structured diagnostic interview for *DSM-IV* personality disorders. It covers 14 *DSM-IV* personality disorder diagnoses, including the 10 standard personality disorders, self-defeating personality disorder, depressive personality disorder, negativistic personality disorder, and mixed personality disorder. Prior to the SIDP-IV structured interview, a full evaluation of the respondent's current mental state is required (Pfohl et al., 1997). This is not surprising given that self-report of enduring personality characteristics can be seriously compromised in a respondent who is experiencing acute psychopathology. Indeed, the aim of all personality assessment measures is to rate the respondent's typical, habitual, and lifelong personal functioning rather than acute or temporary states.

Interestingly, the SIDP-IV does not cover *DSM* personality categories on a disorder-by-disorder basis. Rather, *DSM-IV* personality disorder criteria are reflected in items that are grouped according to 10 topical sections that reflect a different dimension of personality functioning. These sections include interests and activities, work style, close relationships, social relationships, emotions, observational criteria, self-perception, perception of others, stress and anger, and social conformity. These categories are not scored; rather, they reflect broad areas of personal functioning under which personality disorder items can logically be subsumed (Pfohl et al., 1997).

Each SIDP-IV question corresponds to a unique *DSM-IV* personality disorder criterion, except that one item addresses two criteria. An attractive feature is that the specific *DSM-IV* criterion associated with each question is provided for interviewers to easily view. All questions are administered, and there are no options to skip out. Most questions are conversational in tone and open-ended to encourage respondents to talk about their *usual* behaviors and long-term functioning. In fact, respondents are specifically instructed to focus on their typical or habitual behavior when addressing each item and are prompted to "remember what you are like when you are your usual self." Based on client responses, each criterion is rated on a scale with four anchor points. A rating of 0 indicates that the criterion was not present, 1 corresponds to a subthreshold level where there is some evidence of the trait but it is not sufficiently prominent, 2 refers to the criterion being present for most of the past 5 years, and 3 signifies a strongly present and debilitating level. The SIDP-IV requires that a trait be prominent for most of the past 5 years to be considered a part of the respondent's personality. This 5-year rule helps ensure that the particular personality characteristic is stable and of long duration, as required by the General Diagnostic Criteria for Personality Disorders.

A strong point of the organizational format by personality dimensions (rather than by disorders) is that data for specific diagnoses are minimized until final ratings have been collated on the summary sheet. This feature can potentially reduce interviewer biases, such as the halo effect or changing thresholds, if it is obvious that a respondent needs to meet one additional criterion to make the diagnosis. This topical organization also makes the interview's intent less transparent compared to the disorder-by-disorder approach of some other interviews.

Significant clinical judgment is required to properly administer the SIDP-IV, because interviewers are expected to ask additional questions to clarify client responses when necessary. Also, data are not limited to self-report; rather, chart records and significant others such as relatives and friends who know the client well should be consulted when available, and a standard informed consent is included for informant interviews. Such collateral information is particularly prized when evaluating personality-disordered individuals who may lack insight into their own maladaptive personality traits and distort facts about their strengths and limitations. Moreover, informants can also provide diagnostic data that can help resolve the state/trait distinction about specific criterion behaviors.

If discrepancies between sources of information are noted, interviewers must consider all data and use their own judgment to determine the veracity of each source. Making this distinction can be one of the challenges faced by SIDP-IV administrators. Given the multiple sources of diagnostic data, final ratings are made after all sources of information are considered. Such ratings are then transcribed onto a summary sheet that lists each criterion organized by personality disorder, and formal diagnoses are assigned. As required by the *DSM*, diagnoses are made only if the minimum number of criteria (or threshold) has been met for that particular disorder.

Minimum qualifications for competent administration consist of an interviewer with an undergraduate degree in the social sciences and 6 months of experience with diagnostic interviewing. Moreover, an additional month of specialized training and practice with the SIDP is required to become a competent interviewer (Pfohl et al., 1997). Administrators are required to possess an understanding of manifest psychopathology and the typical presentation and course of clinical and personality disorders. Training tapes and workshop information are available from the instrument authors. The SIDP typically requires 60 to 90 minutes for the client interview, 20 minutes for interview of significant informants, and approximately 20 minutes to fill out the summary score sheet. Studies documenting the strong psychometric properties of the SIDP are plentiful, and they are summarized in the manual for the instrument (Pfohl et al., 1997).

THE CULTURAL FORMULATION INTERVIEW (CFI) OF DSM-5

New to *DSM-5* is the Cultural Formulation Interview (CFI), which is a 16-question semistructured interview designed to assess the impact of cultural factors on an individual's mental health. The CFI is based on the Outline for Cultural Formulation, a framework for assessing cultural factors as they relate to individuals' mental health that was first introduced in the *DSM-IV*. Although the CFI is not used to diagnose mental disorders per se, we included it in this chapter because the CFI can be used to understand important cultural issues that can impact the expression and diagnosis of mental disorders in diverse populations.

According to the *DSM-5*, cultural concepts are essential to effective diagnostic assessment and clinical management for several reasons such as:

- Aiding in avoiding misdiagnosis.
- Obtaining useful clinical information.
- Improving clinical rapport and engagement as well as therapeutic efficacy.
- Clarifying cultural epidemiology.
- Guiding clinical research (APA, 2013, p. 759).

The purpose of the CFI is to provide a guide for cultural assessment that improves "cultural validity of diagnostic assessment," aids in treatment planning, and fosters the individual's commitment and satisfaction (APA, 2013). There are two versions of the CFI: the core CFI, which is used to interview the individual, and the CFI-Informant Version, which is used when the individual is unable to answer the question for themselves such as with children, or with persons who are cognitively impaired or psychotic. Information for the CFI-Informant version is collected from a person who knows the individual well and is knowledgeable about the individual's clinical problems, and the person's important life circumstances. The information gathered from the CFI-Informant version can be used as a supplement to, or a replacement for, the core CFI.

The CFI is rooted in a person-centered approach focusing on the individual's perspective of their cultural experiences and social contexts. It is suggested that the CFI be used in conjunction with previously obtained demographic information in order to tailor the questions to the individual's current cultural context (APA, 2013). The information collected from the CFI and or the CFI-Informant version along with all other clinical information should be integrated to create a comprehensive evaluation.

The CFI is composed of four main sections, each focusing on a different aspect of cultural factors encountered in diagnostic assessment. The first section (questions 1–3) focuses on the cultural definition of the problem; the second section (questions 4–10) concentrates on cultural perceptions of cause, contacts, and support; the third section (questions 11–13) focuses on cultural factors affecting self-coping and past help seeking; and finally the fourth section (questions 14–16) focuses on cultural factors affecting current help seeking. The CFI is formatted into two columns. The left-hand column provides information to the interviewer on both how to administer the CFI and the goals of the section. The right-hand column offers suggested questions that can be used in the interview. The CFI is a semistructured interview so the questions are flexible and may be rephrased. Clinicians are also encouraged to ask follow-up questions as needed to clarify individuals' answers. The *DSM-5* suggests that the CFI be used flexibly to maintain a natural flow during the interview and therapeutic rapport (APA, 2013). Additional modules have been created to both guide clinicians who wish to expand on any of the sections and explore them further during the interview and for specific populations such as older adults, children, and immigrants. Supplemental modules can be found online at www.psychiatry.org/dsm5.

SUMMARY AND CONCLUSIONS

This chapter highlights the fact that structured and semistructured interviews have greatly facilitated psychiatric diagnosis, objective measurement of symptoms, and problem clarification in a diverse range of clinical and research settings. Reliability of diagnosis is much improved with the use of structured interviews compared to the nonstandardized approach that is common in clinical practice, and improved reliability provides the foundation for enhanced validity and utility of diagnosis. Given the field's recent emphasis on empirically supported psychotherapeutic interventions and processes (e.g., Barlow, 2014; Castonguay & Beutler, 2006; McHugh & Barlow, 2010; Nathan & Gorman, 2007), we hope that a concomitant focus on clinically relevant,

standardized, objective, and validated assessment procedures will be realized as well. Structured and semistructured interviews play an important role in the advancement of the science of clinical psychology.

This chapter provided a broad overview of the basic issues surrounding structured and semistructured interviews, and it described many interviews available to clinicians and researchers. We hope that this information enables clinicians and researchers to choose instruments that will most appropriately suit their needs. Finally, as noted earlier, with the recent publication of *DSM-5*, many of the structured and semistructured interviews described in this chapter will need to undergo significant revisions to match the classification changes that occurred for many diagnostic categories. The structured and semistructured interviews that are used to diagnose personality disorders do not require imminent revisions because the classification and criteria for the personality disorders did not change from *DSM-IV-TR* to *DSM-5*. The areas of classification and clinical assessment will undoubtedly continue to evolve and change in the coming years. As such, this is an exciting time for researchers and clinicians who use structured and semistructured interviews and other empirically based assessment tools.

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CHAPTER 4

Impact of Race, Ethnicity, and Culture on the Expression and Assessment of Psychopathology

L. KEVIN CHAPMAN, RYAN C. T. DELAPP, and MONNICA T. WILLIAMS

THIS CHAPTER PROVIDES an overview and framework for understanding race, ethnicity, and culture as factors that affect adult psychopathology. Of primary interest are the assessment and treatment of psychopathology that integrates culturally salient values, ideologies, and behaviors into the mental health care of ethnic minorities. Moreover, the chapter is organized into two sections. In the first section, we present a model that highlights relevant multicultural factors that should be considered when working with ethnic minorities. The second section provides a discussion of how to effectively apply the knowledge of these multicultural factors when assessing or treating individuals with diverse ethnic backgrounds. Ultimately, the main objective of this chapter is to encourage mental health professionals to acknowledge the impact of race, ethnicity, and culture on adult psychopathology in order to optimize the efficaciousness of mental health services provided to ethnic minority individuals.

Existing literature has clearly demonstrated the importance of multicultural competency in the assessment and treatment of ethnic minorities. Particularly, the relevance of ethnicity (or "a voluntaristic self-identification with a group culture, identified in terms of language, religion, marriage patterns and real or imaginary origins"; Bradby, 2012, p. 955) in adult psychopathology has been substantiated by evidence identifying disparities in prevalence rates, symptom presentation, and severity, as well as mental health service utilization across diverse ethnic groups. For example, Himle et al. (2009) found that most anxiety disorders (with the exception of PTSD) were more prevalent among non-Hispanic Whites in comparison to African Americans and Caribbean Blacks. However, despite their lower prevalence rates, researchers reported that African Americans and Caribbean Blacks experienced anxiety disorders that were greater in severity and more functionally impairing, which demonstrates how experiences with mental illness can vary by ethnicity.

Moreover, ethnicity has been implicated as a differentiating factor in the diagnosis and treatment of schizophrenia (Fabrega et al., 1994; Gara et al., 2012).

These studies highlight the susceptibility of misdiagnosed schizophrenia in African American patients due to the tendency for African Americans to endorse more psychotic symptoms during diagnostic assessments. As a result, Gara and colleagues (2012) emphasize the importance of culturally sensitive diagnostic assessment tools by explaining how an inability to effectively discriminate schizophrenia and schizoaffective disorders can lead to poor treatment outcomes. Additionally, the relevance of ethnicity in adult psychopathology is bolstered by the findings of Alegría and colleagues (2007), who used data from the National Latino and Asian Study (NLAAS) to identify factors that influence the treatment seeking behaviors of Latino individuals. Specifically, researchers found that the age of migration, Latino ethnicity (e.g., Mexican, Puerto Rican), birth origin (e.g., U.S.-born, foreign-born), primary language spoken, and years of residency in the United States were all influential factors in the use of mental health services and the satisfaction with care received. Most notably, these findings highlight the impact of varied immigration statuses on the perspectives that ethnic minority individuals bring to the mental health arena. Overall, the aforementioned studies clearly underscore the need for multicultural competency in mental health professionals given that one's self-identification with an ethnic heritage has proven to be a vital differentiating factor in the presentation of symptoms and treatment outcomes across diverse adult samples.

RELEVANCE OF ETHNIC IDENTITY AND ACCULTURATION IN ADULT PSYCHOPATHOLOGY

An understanding of the interaction between multicultural factors (e.g., ethnic identity, acculturation) and sociocultural factors (e.g., socioeconomic status, life stress) in ethnic minority patients has become undeniably germane to providing these individuals with effective mental health care. Prior to learning "how" to integrate the understanding of this interaction within assessment, diagnostic, and treatment practices, mental health professionals must possess the knowledge of "what" multicultural factors exist. Accordingly, Carter, Sbrocco, and Carter (1996) have proposed a theoretical model that acknowledges the role of ethnicity, or a "shared culture and lifestyle," as a pivotal underlying construct in the epidemiology, symptom expression, and treatment of psychopathology in ethnic minority individuals (p. 456). Though initially created to explain variations of anxiety disorders in African Americans, the Carter et al. (1996) model can be utilized to more broadly understand the relationship between ethnicity and adult psychopathology by comprehending the salience of ethnic identity and acculturation in all ethnic minorities.

In particular, ethnic identity is a multifarious construct characterized by how people develop and maintain a sense of belonging to their ethnic heritage (Roberts et al., 1999). Important factors influencing a person's ethnic identity include whether they personally identify as a member of an ethnic group, their sentiments and evaluations of the ethnic group, their self-perception of their group membership, their knowledge and commitment to the group, and their ethnic-related behaviors and practices (Burnett-Zeigler, Bohnert, & Ilgen, 2013). Extant literature has provided several models explaining the developmental stages of ethnic identity (Cross, 1978;

Cross & Vandiver, 2001; Phinney, 1989). Collectively, each model describes identity shifts between ethnic ambivalence (lack of interest or pride in one's ethnic background), ethnic exploration (curiosity in one's ethnic background potentially accompanied by a devaluing of other ethnic heritages), and multicultural acceptance (integration of one's commitment to their ethnic background and an appreciation for other ethnic heritages). Evidence supports that individuals high in ethnic identity (i.e., closer to multicultural acceptance) typically have higher levels of self-esteem, develop more protective coping mechanisms, experience more optimism, and report fewer psychological symptoms (Roberts et al., 1999; Smith, Walker, Fields, Brookins, & Seay, 1999; McMahon & Watts, 2002). Notably, Williams, Chapman, Wong, and Turkheimer (2012) compared the relationship between ethnic identity and the psychological symptoms of African American and European American adult samples. Researchers found that higher levels of ethnic identity were related to lower depressive and anxious symptoms in African Americans yet associated with a slight elevation in anxious symptoms for European Americans. Such findings illustrate the protective nature of a strong ethnic identity for minority members. However, some studies suggest that individuals with a strong sense of belonging to their native heritage can amplify the impact of culturally specific stressors (e.g., discrimination; social inequalities), thereby enhancing their focus on their difference from majority culture (Yip, Gee, & Takeuchi, 2008). Past literature has found that the stage of ethnic identity development, age, and level of perceived stress can attenuate the buffering influence of high ethnic identity (see review by Burnett-Zeigler et al., 2013).

Another relevant construct implicated in the Carter et al. (1996) model is acculturation, traditionally defined as the extent to which ethnic minorities adopt the values and participate in the traditional activities of mainstream culture. Recent reconceptualizations of the acculturation process utilize a multidimensional perspective where ethnic minorities must reconcile discrepancies in one's identities (the salience of one's ethnic versus national identity), one's value system (individualism versus collectivism), one's language proficiency, one's cultural attitudes and knowledge, as well as one's cultural practices (Park & Rubin, 2012; Schwartz et al., 2013; Yoon et al., 2013).

According to a meta-analysis of 325 studies about the relationship between acculturation and mental health, Yoon and colleagues (2013) found that mainstream language proficiency was negatively associated with negative mental health, whereas endorsing an ethnic identity was positively related to positive mental health. Most importantly, these findings demonstrate how complex the relationship between acculturation and psychopathology can be, which emphasizes the need for mental health professionals to consider the relevance of each acculturation dimension (e.g., identity, language, value system, behaviors) when working with ethnic minorities. Furthermore, the acculturative stress of integrating disparities in ethnic and mainstream culture across these dimensions can result in difficulties adapting to mainstream culture and/or perceived rejection from one's native heritage (Schwartz et al., 2013), which has been associated with psychopathology in ethnic minority adults (e.g., more eating-disorder symptoms [Van Diest, Tartakovsky, Stachon, Pettit, & Perez, 2013]; greater levels of depression [Driscoll & Torres, 2013; Park & Rubin, 2012]). When confronted with such cultural disparities, extant literature has identified biculturalism, or the ability for ethnic minorities to effectively integrate elements of

two cultural streams, as one of the most protective acculturation statuses against negative health outcomes (Schwartz et al., 2013).

Alternative acculturative statuses include strongly adhering to the mainstream culture and devaluing native heritage (assimilation), strongly adhering to the native heritage and devaluing the mainstream culture (separation), and exhibiting little interest in adhering to either cultural stream (marginalization; see Matsunaga, Hecht, Elek, & Ndiaye, 2010; Yoon et al., 2013). Overall, existing literature has yielded inconclusive findings clarifying the impact of acculturation on the mental health of ethnic minorities (see Concepcion, Kohatsu, & Yeh, 2013), which has been accredited to the multiple definitions of acculturation (e.g., time since immigration, language fluency, acculturation status) and examining this construct in few ethnic minority groups (Burnett-Zeigler et al., 2013; Yoon et al., 2013).

Aside from having knowledge of ethnic identity and acculturation, mental health professionals must also understand how these constructs interact to influence the psychopathology expressed in many ethnic minority individuals (Yoon et al., 2013). In referencing the Carter et al. (1996) model, African Americans who maintain a strong ethnic identity and are highly assimilated in the dominant culture are believed to endorse traditional beliefs of mainstream society (e.g., individualism) and exhibit symptoms presentations consistent with the current diagnostic nomenclature. Notably, it is theorized that these individuals may feel conflicted by being acculturated to believe psychological treatment is effective while embodying a mistrust of societal systems in mainstream culture as a result of historically significant cultural experiences (e.g., perceived discrimination from individuals of the dominant culture). Similarly, Carter et al. (1996) conceptualized that African Americans low in ethnic identity yet highly assimilated will exhibit a traditional symptom presentation, but be more willing to seek, persist through, and benefit from traditional treatment practices. In contrast, individuals high in ethnic identity who strongly de-identify with mainstream culture (separation acculturation status) represent a subset of ethnic minorities who may display unique symptom presentations and utilize culturally specific explanations for their symptoms, thereby resulting in a greater likelihood for misdiagnosed psychopathology. Further, these individuals are theorized to be less likely to seek treatment due to mistrust in and/or a limited knowledge of mental health care.

Although there is a dearth of literature devoted to examining the additive impact of ethnic identity and acculturation on adult psychopathology (Chae & Foley, 2010), several studies provide evidence supporting the broad application of the Carter et al. (1996) model across diverse ethnic minority groups. Burnett-Zeigler et al. (2013) examined the relationship between ethnic identity, acculturation, and the lifetime prevalence of mental illness and substance use in African American, Latino, and Asian samples. Results indicated that higher levels of ethnic identity, and not higher acculturation, were related to decreased lifetime prevalence of psychiatric illness and substance use for each minority group. Notably, higher acculturation (e.g., use of English language or social preference for individuals not in ethnic group) was associated with increased prevalence of depression in African Americans and Hispanics, increased bipolar diagnoses in Hispanics, and increased anxiety disorder diagnoses for all minority groups. Regarding substance use, higher acculturation was related to increased lifetime prevalence of alcohol and drug use among the Hispanic and Asian sample. These findings suggest that having a strong sense of pride and

belonging to an ethnic heritage is protective; however, nondominant individuals who are unable to maintain cultural ties with their native heritage (e.g., first language, relationships with members of ethnic group) may be more susceptible to negative health outcomes.

Nascent literature has provided a more specific understanding of the interaction between these two constructs by utilizing acculturation statuses (e.g., integration, assimilation, separation) instead of a broad definition of acculturation (e.g., English literacy; time of residency). In particular, Matsunga and colleagues examined the interaction between ethnic identity and acculturation status in Mexican-heritage adolescents living in the southwest region of the United States and found that an integration acculturation status was more prevalent than assimilation as well as more predictive of a strong ethnic identification (Matsunaga et al., 2010), which suggests that a strong ethnic identity and a successful integration of two cultures are closely associated. Furthermore, Chae and Foley (2010) found that high ethnic identity strongly predicted positive psychological well-being among Chinese, Japanese, and Korean Americans whereas an assimilation acculturation status predicted poorer psychological well-being among Korean Americans. Also, researchers found that Asian Americans with an integration acculturation status experienced significantly higher psychological well-being compared to other acculturation statuses. Most importantly, these findings suggest that ethnic minorities who maintain a strong sense of belonging to their ethnic heritage (high ethnic identity) and who have successfully integrated the identities, value systems, and cultural practices of their native and mainstream heritages (integration) exhibit fewer clinical symptoms and more life satisfaction.

RELEVANCE OF SOCIOCULTURAL FACTORS IN ADULT PSYCHOPATHOLOGY

Though an understanding of the aforementioned constructs is essential, it is equally important to examine the impact of other sociocultural variables that also exert a considerable degree of influence over the symptom presentation and treatment outcomes of ethnic minorities. Although extant literature has identified a myriad of variables that impact minority mental health, the current chapter solely focuses on socioeconomic status (SES), stressful life events, and age cohort, which were each identified by the Carter et al. (1996) model as important contributors to the mental health of ethnic minorities.

Researchers propose that SES can provide a more precise understanding of the relationship between ethnicity and adult psychopathology by focusing on the specific environmental elements that characterize each social class. Past literature has shown that high SES is related to better health outcomes. One study by Shen and Takeuchi (2001) examining the relationship between acculturation, SES, and depression in Chinese Americans found that SES was a better indicator of depressive symptoms than acculturation and that high SES individuals (i.e., high educational attainment and increased income) were related to better mental health outcome (i.e., fewer depressive symptoms) compared to low SES individuals. These findings suggest that it is through the variance in SES and related variables (e.g., perceptions of stress, social support, and physical health) that acculturation may impact the mental health

of nondominant individuals (Shen & Takeuchi, 2001). Contrarily, nascent literature has begun to propose that the association between social class and mental health is much more complex in that evidence has supported that low SES and/or foreign-born individuals are not automatically guaranteed poor health outcomes (John, de Castro, Martin, Duran, & Takeuchi, 2012). Given such findings, it suggests that mental health professionals should acknowledge the detrimental as well as the protective elements of one's social class.

Also, the Carter et al. (1996) model identifies stressful life events as a contributor to the variability in the psychopathology of ethnic minorities. Though a comprehensive understanding of the multiple forms of stress (e.g., violence exposures, neighborhood context, poverty, etc.) is beyond the scope of this chapter, extant literature pinpoints race/ethnic-based stress as influential to the mental health of ethnic minority individuals. In particular, Greer (2011) describes racism as "complex systems of privilege and power, which ultimately serve to threaten and/or exclude racial and ethnic minorities from access to societal resources and other civil liberties" (p. 215). As a result of such racial/ethnic injustice, many ethnic minorities are subjected to damaging race/ethnic-focused attitudinal appraisals (i.e., prejudice), race/ethnic-focused assumptions (i.e., stereotypes), and unjust treatment based upon their race/ethnicity (Greer, 2011).

Past studies have indicated that exposure to such race/ethnic-based experiences are strong indicators of mental health outcomes across diverse ethnic minority groups (e.g., discrimination was related to increased lifetime prevalence of generalized anxiety disorder in African Americans [Soto, Dawson-Andoh, & BeLue, 2011]; perceived discrimination was associated with increased anxiety, affective, substance abuse disorders among African Americans, Hispanic Americans, and Asian Americans [Chou, Asnaani, & Hofmann, 2012]). Notably, empirical evidence suggests that perceived discrimination may be particularly salient to African American clients, given that several studies have found African Americans to endorse greater degrees of perceived discrimination in comparison to other ethnic minority groups in the United States (Cokley, Hall-Clark, & Hicks, 2011; Donovan, Huynh, Park, Kim, Lee, & Robertson, 2013). Overall, when utilizing ethnic identity and acculturation to gain insight into the culturally specific worldviews of nondominant individuals, it is imperative that mental health professionals also examine the occurrence and impact of race/ethnic-based stressors on the psychopathology of ethnic minorities.

Finally, the Carter et al. (1996) model discusses the relevance of age cohort in the manifestation of psychopathology in ethnic minorities. The evolution of the "social, economic, and political climate" in the United States has yielded diverse experiences across generations of ethnic minorities in this country, thereby impacting the meaning of ethnicity for each generation (Carter et al., 1996, p. 460). In the context of each ethnic group, there are different historical details separating each generation; however, the impact of age cohort on psychopathology remains a relevant consideration. In general, existing literature has implicated intergenerational disparities in perceived racial discrimination (Yip et al., 2008), ethnic identity (Yip et al., 2008), acculturation status (Buscemi, Williams, Tappen, & Blais, 2012), and lifetime prevalence of psychiatric illness (Breslau, Aguilar-Gaxiola, Kendler, Su, Williams, & Kessler, 2006) across the adult lifespan. One study particularly relevant to this chapter's discussion of the Carter et al. (1996) model examined the protective and/or exacerbating nature of

ethnic identity in the relationship between racial discrimination and psychological distress in Asian adults (Yip et al., 2008). Results indicated that ethnic identity appeared to buffer the negative impact of racial discrimination on the psychological distress for adults ages 41 to 50 yet exacerbate the effects of racial discrimination for adults ages 31 to 40 and 51 and older. In an attempt to explain these findings, Yip and colleagues (2008) theorize that the former age cohort is more likely to have a stable lifestyle with more coping mechanisms for stress, whereas the latter age cohorts may characterize adults who are in the exploration phase of their ethnic identity, which, therefore, heightens their sensitivity to being unfairly treated on the basis of their race/ethnicity. Furthermore, the parent-child relationship is another important way that intergenerational differences can impact adult psychopathology, especially for immigrant families (Kim, 2011; Vu & Rook, 2012).

In a study examining intergenerational acculturation conflict and depressive symptoms among Korean American parents, Kim (2011) found that greater discrepancies in cultural values between parent and child (greater intergenerational conflict) was related to increased parental depressive symptoms; an association more pronounced in mothers compared to fathers. It was proposed that the cultural expectations of the Korean mother (e.g., to be a "wise and benevolent" primary care giver) was conflicted by an incongruence with the value system of mainstream culture (Kim, 2011, p. 691). Collectively, such findings provide evidence that the Carter et al. (1996) model elucidates culturally specific considerations for psychological distress among diverse ethnic minorities.

SECTION 2: APPLICATION OF MULTICULTURAL FACTORS

Prior to addressing how the aforementioned factors can be applied to enhance the efficiency and effectiveness of treatment in ethnic minority patients, it is equally important to understand how culture, race, and ethnicity impact the evaluation of psychopathology within such populations. In the following section, the pertinence of validating assessment tools among ethnic minority groups is discussed. In particular, there is a general overview of common statistical methods used to establish measurement equivalence across diverse groups as well as important considerations when translating the results of such statistical methods to the in vivo assessment of ethnic minority clients.

Assessment

Historically, there has been a ubiquitous disconnect between investigating various facets of theoretical models that are endemic to ethnic minority populations, and the subsequent application of these constructs in practice. As mentioned earlier, there are a number of unique, culturally specific factors that undoubtedly influence the manifestation (and subsequent treatment) of various forms of psychopathology. There is a substantive literature underscoring the exigency for conducting translational research in ethnic minority populations that are beyond the scope of this chapter (for a review, see Hofmann & Parron, 1996; Nagayama Hall, 2001). Worth noting, however, are two relatively salient implications from the empirical literature. First, the need for culturally sensitive assessment tools that aid in the diagnosis of psychopathology in

ethnic minority individuals. Second, the need for investigators to delineate ingredients for culturally sensitive interventions, presumably as a result of uncovering culturally specific factors through rigorous assessment in ethnic-minority populations.

As noted in the previous edition of this chapter, establishing measurement equivalence (or lack thereof) is paramount before proceeding with effective translational research, particularly as it relates to ethnic minority populations. In the previous edition, the authors described (a) linguistic/translation equivalence (accuracy of translation/understanding from the perspective of the ethnic minority individual), (b) conceptual equivalence (whether the underlying construct maintains the same meaning in ethnic minority individuals as in European Americans), and (c) psychometric equivalence (whether the construct is measured the same across groups). Given that the previous edition provided readers with a thorough overview of the various components of measurement equivalence, the scope of the current chapter is to highlight more recent work in the area of measurement equivalence with the aim of delineating potential "ingredients" for culturally sensitive assessment tools in ethnic minority populations. Only a brief summary is provided in this edition.

The most important prerequisite to assessment with ethnic minority populations is taking a multicultural perspective rather than an ethnocentric one. In short, multiculturalism refers to the recognition of equality of various cultural groups and the right of individuals to follow their own specified paths (Shiraev & Levy, 2013). Ethnocentrism, on the other hand, refers to a cognitive bias that supports "judgment about other ethnic, national and cultural groups from the observer's perspective" (Shiraev & Levy, 2013, p. 19). Along these lines, when considering linguistic translation equivalence, one point worth noting is that evaluators must remain cognizant of the cognitive biases that we all possess and subsequently acknowledge that our literacy is culturally based (Shiraev & Levy, 2013).

Although many concepts translate naturally across cultures (e.g., numbers), scientists and practitioners need to be increasingly mindful of the interplay between culture, race, and ethnicity during *all* types of assessment. As previously noted, differences in racial identity, age, participation in acculturation experiences, and environment could significantly impact how many ethnic minority individuals respond to questions on a particular measure. Generally agreed upon standards have been established when language differences exist, particularly as it relates to forward and backward translation (e.g., Butcher, 1996). Appropriately trained, bilingual administrators are critically important when establishing linguistic translation equivalence.

More recently, significant strides have been made in the realm of conceptual and psychometric equivalence across racial and ethnic minority groups. Beyond basic theory, the question of conceptual equivalence can most accurately be investigated by determining psychometric equivalence. As such, it should be noted that the lack of either conceptual or psychometric equivalence neither precludes the elimination of an assessment tool nor suggests that the measure is not useful with a given ethnic minority population. Depending on the properties of the given measure, results of statistical analyses may suggest the necessity to modify the assessment tool into a more effective screener as a precursor for further diagnostic assessment (detailed later). Nonetheless, psychometric equivalence is arguably the most important standard to establish in order to fully understand how to proceed with assessment and subsequent treatment geared toward ethnic minority individuals.

Before proceeding, it is important to reemphasize the importance of heterogeneity in ethnic minority individuals and the relative differences in racial identity, acculturation, and the other previously described sociocultural constructs that influence the assessment experience. Historically, the exception during assessment has been to be mindful of cultural heterogeneity prior to assessment when, in fact, the understanding of this heterogeneity is most accurately described as the rule. Moreover, we are reemphasizing the importance of assessing relevant sociocultural variables as a preamble to the discussion of a very promising area of investigation in ethnic minority assessment and treatment, specifically, factor pattern analyses with certain measures.

Factor Pattern Investigations in Ethnic Minorities

Perhaps the most promising investigations in this area are the nascent, factor analytic studies that examine factor patterns across racial and ethnic minority groups, particularly in the realm of anxiety and related disorders. The majority of these investigations have utilized structural equation modeling (SEM), a comprehensive yet flexible approach that allows the investigator to examine various relationships among variables while controlling for measurement error (see Bentler, 1990; Hu & Bentler, 1999). The ability of an investigator to control for measurement area when examining measurement equivalence while simultaneously examining various components of the general linear model makes this approach very attractive over traditional analytic methods.

Many investigators interested in the assessment and treatment of ethnic minority individuals have employed SEM in order to determine whether commonly used assessment tools are equivalent (or contain invariant factor patterns) across European American individuals (the majority in the United States) and ethnic minority individuals. The most commonly used method for making this determination is one facet of the SEM, confirmatory factor analysis (CFA) also referred to as the "measurement model" (Hoyle & Smith, 1994). In other words, does the construct that is purportedly measured by "X" tool in European Americans yield the same results in a specific ethnic minority population? Several studies have yielded promising results related to psychometric equivalence for various tools in the anxiety disorders literature for use with ethnic minority populations. For instance, Chapman, Petrie, and Vines (2012) found that the factor structure of the Symptom Checklist 90–Revised (SCL-90-R), a commonly utilized measure of psychological distress, was equivalent in a sample of African American females. These results suggest that the SCL-90-R in its current form has established empirical support for utilization in a community sample of African American females.

Other studies have examined measurement equivalence using similar methodology with disparate findings when utilizing different measures. As mentioned earlier, factor *variance* does not preclude the elimination of a measure; rather it may suggest the need for a *modified* version of the measure. For instance, Melka and colleagues (Melka, Lancaster, Adams, Howarth, & Rodriguez, 2010) examined the Fear of Negative Evaluation Scale (FNE) and the Social Avoidance and Distress Scale (SAD) in a sample of non-Hispanic White and African American young adults and found that several items on both measures needed to be omitted for the African American sample. Similarly, Chapman, Williams, Mast, and Woodruff-Borden (2009)

investigated the original and other extant factor structures of the Beck Anxiety Inventory (BAI), arguably the most widely used self-report measure for anxiety symptoms in general, in a sample of African American and non-Hispanic White adults. Results revealed that the original factor structure was not equivalent in the African American sample and that a 19-item version of the BAI best fit the African American sample (Chapman et al., 2009). Similar results have been obtained with other, widely utilized measures of family functioning (Family Assessment Device; Chapman & Woodruff-Borden, 2009), specific phobias (Chapman, Kertz, Zurlage, & Woodruff-Borden, 2008; Chapman, Vines, & Petrie, 2011), and perceived control over anxiety (Chapman, Kertz, & Woodruff-Borden, 2009), further underscoring the importance of understanding cultural factors related to assessment in ethnic minority individuals.

Clinical Utility Assessment in Ethnic Minorities

In attempts to further understand which assessment tools have adequate clinical utility in ethnic minority samples, other investigators have employed statistical techniques aimed at predicting the presence of psychopathology from screening tools. The extent to which screening tools are sensitive at predicting the presence or absence of a specific disorder, particularly in ethnic minority populations, has a number of implications for clinical work. In short, the assessment process may be streamlined through early detection of disorders, which in turn allows the clinician to spend more time in (a) building rapport with ethnic minority clients and (b) engaging in time-limited, clinical intervention. Along these lines, a receiver operating characteristic analysis (ROC) is one such method that has been heavily utilized to predict the presence of various medical conditions (e.g., diagnosing breast cancer via digital mammograms [Cole et al., 2004]; pneumonia detection [Lynch, Platt, Gouin, Larson, & Patenaude, 2004]) and psychiatric conditions (e.g., dexamethosone suppression test for predicting major depressive disorder [Mossman & Somoza, 1989]; harm avoidance scores predicting generalized anxiety disorder [Rettew, Doyle, Kwan, Stanger, & Hudziak, 2006]; predicting PTSD with PTSD Checklist in female veterans [Lang, Laffaye, Satz, Dresselhaus, & Stein, 2003]).

Although a description of a ROC analysis is beyond the scope of this chapter, worth noting is that the ROC analysis calculates an area under the curve (AUC), which determines the suitability of a given measure as a screening tool, because it reflects the likelihood that a participant who meets criteria for a diagnosis selected at random will score higher on a measure than a randomly selected control participant (see Bredemeier et al., 2010). Moreover, a ROC analysis provides optimal cut scores for specific measures in predicting the presence of particular disorders. In a more recent investigation, Petrie, Chapman, and Vines (2013) investigated the sensitivity and specificity of the Positive and Negative Affect Scales Expanded Form (PANAS-X) at detecting social anxiety disorder in a sample of African American women. Results suggest that the PANAS-X is a clinically useful measure at predicting social anxiety disorder in African American females. More specifically, a score above 11 on the Negative Affect Scale of the PANAS-X indicates further examination (e.g., a diagnostic interview) is warranted to assess the presence of social-anxiety disorder, whereas a score below 35 on the Positive Affect Scale reveals the need for further

examination to determine the presence of *any* anxiety disorder. Chapman, Petrie, and Richards (under review) yielded similar results with other measures predicting social anxiety disorder, specifically for the Social Phobia Scale (SPS; cut score of 6>), Albany Panic and Phobia Questionnaire (APPQ; score of 7>), Social Interaction Scale (SIAS; cut score of 15>), and a social "fear factor" from the Fear Survey Schedule–Second Edition (FSS-II; cut score of 7>). It should be noted that the social "fear factor" (see Chapman et al., 2008; Chapman et al., 2011) is composed of only four items.

Taken together, these results suggest that the assessment of sociocultural factors at the beginning of treatment in addition to the utilization of assessment measures that demonstrate clinical utility in ethnic minority samples (or when modification is necessary) is critically important to effective assessment. Readers are encouraged to further explore the aforementioned measures to further determine their clinical utility in ethnic minority samples.

EXPRESSION/ASSESSMENT OF PSYCHOPATHOLOGY

Aside from the administration of culturally sensitive assessment tools to aid in the accurate diagnosis of psychopathology among ethnic minority patients, extant literature has implicated cultural factors endemic to ethnic groups that may influence the expression of their symptomology. In the following section, a general overview of how factors, such as perceived discrimination and stigma of mental illness, impact various forms of symptom expression among non-Western and Western ethnic groups is presented.

Expression of Psychopathology Differs Across Cultural Groups

It is often unclear how symptom profiles may differ between ethnic groups when typical research studies use structured instruments, based on an a priori set of questions believed to exemplify the disorder under investigation (Guarnaccia, 1997). Measures based on Western notions of prototypical symptoms will fail to capture cultural differences in the expression of all disorders. Thus, variations in symptom patterns are often overlooked or misunderstood. Such misunderstandings affect how we, in turn, conceptualize even seemingly well-defined disorders.

The *DSM-5* recognizes several cultural concepts of distress, or mental disorders that are generally limited to specific cultural groups for certain dysfunctional and/or distressing behaviors, experiences, and observations (American Psychiatric Association, 2013). However, many culture-bound syndromes are likely unrecognized variations of common Western ailments. For example, susto is a Latin American folk illness attributed to having an extremely frightening experience, thought to include "soul loss" as part of the syndrome. People afflicted with susto may have symptoms that include nervousness, loss of appetite, insomnia, listlessness, despondency, involuntary muscle tics, and diarrhea. The symptoms of susto are actually quite similar to posttraumatic stress disorder (PTSD), which includes anxiety, avoidance, dissociation, jumpiness, sleep disturbances, and depression. When referring to soul loss within susto, a closer meaning to this may actually be loss of "vital force," as the soul is typically not thought to have actually left the body until death (Glazer, Baer, Weller, Garcia de Alba, & Liebowitz, 2004). This could resemble the fatigue and

anhedonia, which may be a part of depressive symptoms within PTSD. Additionally, feeling as if one's soul has been lost may be an idiom of distress for dissociation. Therefore, the concept of susto as a culture-bound syndrome may be better conceptualized as a culture-specific description of PTSD itself.

Interestingly, folk treatments for the disorder include elements of exposure-based therapies for PTSD (e.g., Williams, Cahill, & Foa, 2010). During the treatment ritual, the individual afflicted with susto must recount their terrifying experience while lying on the axis of a crucifix on the floor. Fresh herbs are swept over the afflicted individual's body while the folk healer says a series of prayers (Gillette, 2013). Sugar, water, and tea may also be used (Glazer et al., 2004). If the first session is not effective, the process is repeated every third day until the patient is recovered. This repeated recounting process is a critical active ingredient in prolonged exposure, a highly effective treatment for PTSD developed by Foa, Hembree, and Rothbaum (2007), and likely accounts for the effectiveness of the folk remedy.

Another example of the connection between *DSM* disorders and culture-bound syndromes can be seen in the enigmatic ailment called koro. Though uncommon in Western cultures, koro is characterized by anxiety over the possibility of one's genitalia receding into the body, resulting in infertility or death (Chowdhury, 1990). To prevent any envisioned shrinkage or retraction of the genitals, a koro sufferer will perform certain behaviors (i.e., pulling of genitals, spiritual rituals, securing genitals to prevent retraction) intended to reduce or eliminate this risk.

Obsessive-compulsive disorder (OCD) is characterized by distressing and typically implausible obsessions, with compulsions designed to reduce the anxiety caused by the obsessions. Davis, Steever, Terwilliger, & Williams (2012) note the possibility that koro is simply a form of OCD, as an alternative to the current classification as a culture-bound syndrome. The most salient feature of koro concerns the anxiety surrounding the retraction and shrinkage of genitalia. The degree to which this distress can impair the daily functioning of those with koro has marked similarities to the construct of obsessions in OCD. This, coupled with the improbability of one's genitalia actually receding into one's body, makes it possible to categorize this fear as an obsession.

Sexual obsessions are extremely common in OCD worldwide (Williams & Steever, in press), but these types of thoughts are considered taboo or embarrassing in most cultures. Thus, the stigma and shame attached to the experience of sexual symptoms of OCD is highly distressing (Gordon, 2002). Furthermore, Bernstein and Gaw (1990) note that sexual identity questions and conflicting feelings about sexuality are common in the experience of koro. Similarly, approximately 10% of treatment-seeking OCD patients report concerns about their sexual identity as a main concern (Williams & Farris, 2011). In OCD, these worries often manifest as fears of experiencing a change in sexual orientation, which is strikingly similar to the worries reported to underlie many cases of koro. Finally, koro has been shown to respond well to behavioral psychotherapy and medications like selective serotonin reuptake inhibitors (SSRIs; Buckle, Chuah, Fones, & Wong, 2007). These same treatments have long been the preferred method of treatment for OCD and its subtypes (e.g., NICE, 2005). Thus, koro is likely simply a cultural variant of OCD.

Although listed in *DSM-5* as a culture-bound syndrome, neurasthenia, or shenjing shuairuo, is currently a recognized mental disorder in the World Health Organization's *ICD-10* and in the Chinese Classification of Mental Disorders. Traditional

Chinese medicine describes shenjing shuairuo as a depletion of vital energy and reduced functioning in critical internal organs. The Chinese Classification of Mental Disorders considers it a mental disorder that may include weakness, emotional symptoms, excitement symptoms, tension-induced pain, and sleep disturbances. Neurasthenia has been considered a somatic illness, similar to or the same as major depressive disorder, but involving culturally sanctioned idioms of distress (Shiraev & Levy, 2013).

Likewise, there are many conditions that may be considered Western culture-bound syndromes, due to their infrequency or absence in other cultures. These may include: anorexia nervosa, adolescence, drug abuse, chronic fatigue syndrome, animal hoarding, ADHD, Munchhausen by proxy, premenstrual syndromes, dissociative identity disorder, and even Type A personality. Many maintain that all psychiatric disorders, regardless of culture, are always culturally influenced constructs. Still others assert that the *DSM* is in itself a culture-bound document and question whether it should be used at all outside its country of origin (Nadkarni & Santhouse, 2012).

Expression of Psychopathology Differs Within National Borders

It may be misleading to present cultural differences in psychopathology as an issue only applicable to those in non-Western or developing nations. The expression of psychopathology can and does differ among U.S. ethnic groups that may be considered fairly acculturated (i.e., that share a common language and national borders).

For example, African Americans have been an integral part of American life for centuries, yet notable differences in psychopathology are nonetheless evident. A recent investigation of OCD in African Americans (Williams, Elstein, Buckner, Abelson, & Himle, 2012) found obsessive-compulsive concerns in six major areas, including (1) contamination and washing, (2) hoarding, (3) sexual obsessions and reassurance, (4) aggression and mental compulsions, (5) symmetry and perfectionism, and (6) doubt and checking. These dimensions are similar to findings of studies in primarily White samples (i.e., Bloch et al., 2008). However, African Americans with OCD report more contamination symptoms and were twice as likely to report excessive concerns with animals compared to European Americans with OCD. This indicates notable cultural differences, which is consistent with findings among nonclinical samples (e.g., Thomas, Turkheimer, & Oltmanns, 2000).

Williams and Turkheimer (2007) studied racial differences in OCD symptoms and found that a nonclinical sample of African Americans scored significantly higher on an animal attitude factor than European Americans, meaning they had greater concerns about animals, and it was determined that cultural factors explained this difference. It was hypothesized that the Western perspective of animals as pets is more socially acceptable among European Americans than other cultures that are more likely to regard animals as a source of food or vehicle for labor. Other cultural differences may relate to the historic practices such as the use of dogs as a means to hunt slaves or attack protesters during the Civil Rights era. This is consistent with recent work suggesting that African Americans may experience greater phobias of animals (Chapman et al., 2008). As such, cultural differences are plausible contributing factors for increased animal sensitivity among those with OCD.

Fear of being misunderstood was also more frequently endorsed by African Americans with OCD (Williams et al., 2012). An obsessive need to be perfectly understood could be a unique finding for African Americans related to fears of appearing unintelligent, resulting in *stereotype compensation*—an intentional effort to present oneself in a counterstereotypical manner (Williams, Turkheimer, Magee, & Guterbock, 2008).

Prevalence Rates May Differ for Cultural Reasons

Prevalence rates of various disorders also may differ for cultural reasons. For example, the National Survey of American Life (NSAL) conducted a comprehensive nationwide study of African American and Caribbean Blacks. They interviewed a large number of adults ($n = 5{,}191$) and adolescents ($n = 1{,}170$) in their homes, using professionally trained, ethnically matched interviewers. Their study was the first to examine the prevalence, age of onset, and gender differences in a number of mental disorders in a nationally representative Black sample (Taylor, Caldwell, Baser, Faison, & Jackson, 2007).

Findings were consistent with previous research indicating that anorexia nervosa is rare among African Americans. In fact, not a single woman in the study met criteria for anorexia in the previous 12 months, and there were no reports at all of anorexia in Caribbean adults. These findings indicate that Black Americans are at lower risk of anorexia than their White counterparts. Likewise, a related study found that Hispanic and Asian American female adults experienced similarly low rates of anorexia nervosa (Franko, 2007). The authors of that study suggested that detection and barriers to treatment may be a factor in the lower rates, but there has been very little research focused on what cultural factors may differentially protect minorities from this disorder and yet promote it in European Americans.

Another way that culture may impact psychopathology can be found in the frequencies of specific symptoms within a disorder. For example, Chapman and colleagues (Chapman et al., 2008; Chapman et al., 2011) found that both African American college students (2008) and African American adults from the community (2011) reported more animal and social fears than their European American counterparts. These results indicate the need for further exploration of cultural factors and their impact on psychopathology.

Stigma and Somatization of Distress Across Cultures

Although there is a general tendency toward somatization across all cultures, ethnic minority individuals in the United States appear more likely to express psychological distress through bodily symptoms for two primary reasons: (1) as compared to European Americans, there is a higher level of stigma associated with mental illness and, therefore, physical symptoms are more socially acceptable, and (2) there is more holistic conceptualization of the person, and, therefore, less of a distinction between mind and body among ethnic minorities (USDHHS, 2001).

For many groups there is considerable stigma attached to being afflicted by mental illness, and thus clients from these groups may be more comfortable reporting physical symptoms over affective and cognitive symptoms. One study of African

Americans found that concerns about stigma prompted most mental health care consumers to initially avoid or delay treatment, and once in treatment, they commonly faced stigmatizing reactions from others (Alvidrez, Snowden, & Kaiser, 2008). Hunter and Schmidt (2010) developed a model that incorporates stigma, racism, and somatization into the expression of anxiety in African Americans. The emphasis on physical illnesses over mental illness in African American communities is thought to be related to physical explanations of somatic symptoms of anxiety, including attributing these to conditions like cardiovascular disease, and subsequent help seeking oriented to these explanations. In particular, anxiety disorders among African Americans are likely to include both fears related to minority status and catastrophic interpretations of somatic symptoms. They propose that these differences, because of their implications for measurement and diagnosis, can explain reduced detection of certain anxiety disorders in African Americans compared with European Americans.

Western models of health and illness often depict a fragmented representation of the person to conceptualize mental and physical processes. For example the mind and body are regarded as separate (called *dualism*), and then the mind is even further divided in many common models (e.g., psychodynamic personality model of id, ego, and superego; cognitive behavioral therapy's affective, behavioral, and cognitive components). However, many cultures do not make a distinction between the mind and body. Additionally, many cultural traditions recognize the spirit as an integral part of the person, inseparable from the mind and body (e.g., Parham, 2002). Thus, omitting this component will reduce the salience of the treatment in such clients.

Spirituality and Religion

Spirituality and religious beliefs can be the most important facets of a person's identity, thus appreciating spiritual and religious diversity is essential to multicultural competency. In North America, 97% of adults profess spiritual beliefs, and 85% of the population is Christian; of these, 65% say their beliefs are central to their lives (Shiraev & Levy, 2013). When help is sought, clients typically look for someone who shares the same values. Thus, therapists will be viewed as more credible in the community if competent in religious/spiritual issues.

Devout or orthodox members of most religious traditions tend to have negative perceptions of the mental health professions, distrust therapists, and underutilize mental health services. This is in part because traditionally the field of psychology has been hostile toward religion. Psychologists are more secular and less religious than the population at large, and therapists have tended to reject organized religious involvement; thus, there is a religiosity gap between mental health providers and the U.S. majority. As a result, building trust may be challenging when working with devout clients, and, in such cases, learning about a client's religious tradition is essential to building rapport. At the very least, it is essential for therapists to avoid interventions that conflict with normative religious beliefs. Therapists need to be able to understand individuals and their beliefs within their cultural context (Richards, Keller, & Smith, 2004).

Over the past few years, an uneasy truce has developed between psychology and religion. This is due in part to new research that shows the important role of religion in

mental health and well-being. For example, meditation and prayer are correlated with reduced blood pressure and pulse, lower endocrine activity, and lower metabolism. Religious involvement has also been shown to buffer against emotional difficulties, such as depression and anger. Thus a variety of psychological and spiritual interventions may be appropriate with religious clients, depending on the client, the nature of the problem, and the therapist's religious affiliation.

Racism and Discrimination

As previously noted, the experience of being a stigmatized ethnoracial minority is a common phenomenon across cultures, with profound implications for mental health. This includes visible minorities in the United States and Canada, as well as ethnic and cultural groups in other countries, such as Blacks in the United Kingdom, Turks in Germany, and the Dalit in India. Many studies have established a link between discrimination and mental health outcomes. In the United States, African Americans experience the most racial discrimination, followed by Asian Americans and Hispanic Americans (Chou et al., 2012). Perceived discrimination has been found to be negatively correlated with mental health, and the effects seem to be strongest (most detrimental) for Asian Americans, followed by Hispanic Americans, followed by African Americans (Cokley, Hall-Clark, & Hicks, 2011).

In addition to overall psychological distress, racism and discrimination have been associated with several specific mental health problems, including stress (Clark, Anderson, Clark, & Williams, 1999), depression (Banks & Kohn-Wood, 2007; Torres, Driscoll, & Burrow, 2010), anxiety (Hunter & Schmidt, 2010), binge drinking (Blume, Lovato, Thyken, & Denny, 2012), and PTSD (Carter, 2007; Pieterse, Todd, Neville, & Carter, 2012). A strong, positive ethnic identity has been shown to be a potential protective factor against psychopathology among minorities (e.g., Williams, Chapman, et al., 2012), except when discriminatory events are severe (Chae, Lincoln, & Jackson, 2011). Failure to understand the role of racism and discrimination limits our understanding of mental health in stigmatized people groups.

Focusing specifically on the link between racism and PTSD can help us understand how Eurocentric models may sometimes be inadequate for identifying distress in minority populations. The criteria for a PTSD diagnosis implies that a traumatizing event must be negative and uncontrollable, whereby an individual's physical well-being is threatened (American Psychiatric Association, 2000). Although this description may address many forms of ethnoracially motivated traumatic events, it does not take into account ongoing low levels of racism that can lead to a general sense of distress and uncontrollability (Carter, 2007). These experiences, though they may not be physical in nature, attack the individual's identity and force the person to re-experience traumas associated with their culture's history (Helms, Nicholas, & Green, 2010).

Previous editions of the *DSM* recognized racism as trauma only when an individual met criteria for PTSD in relation to a discrete racist event. This is problematic given that many minorities experience cumulative experiences of racism as traumatic, with a discrete event acting as "the last straw" triggering trauma reactions (Carter, 2007). Thus, current conceptualizations of trauma as a discrete horrific event may be limiting for minorities. Recent changes to the *DSM* may open the door for wider recognition of

racism-related trauma. It is now within criteria that a person can have PTSD from learning about a traumatic event involving a close friend or family member, or if a person is repeatedly exposed to details about trauma (APA, 2013). This could encompass trauma resulting from ongoing racial stressors (Malcoun, Williams, & Bahojb Nouri, in press).

Moreover, existing PTSD measures aimed at identifying an index trauma fail to include racism among listed choice response options, leaving such events to be reported as "other" or made to fit into an existing category that may not fully capture the nature of the trauma (e.g., physical assault). This can be especially problematic since minorities may be reluctant to report experiences of racism to European American therapists (Carter, 2007), who comprise the majority of mental health clinicians in the United States (U.S. Department of Labor, 2012). Minority clients also may not link current PTSD symptoms to a single experience of racism if their symptoms relate to cumulative experiences of discrimination.

Bryant-Davis and Ocampo (2005) noted the similar courses of psychopathology between rape victims and victims of racism. Similar to rape victims, race-related trauma victims may respond with dissociation or shock, which can prevent them from responding to the incident in a functional manner. Victims may then feel shame and self-blame because they were unable to respond or defend themselves, which may lead to poor self-concept or self-destructive behaviors (Bryant-Davis & Ocampo, 2005). In the same investigation, a parallel was drawn between race-related trauma victims and victims of domestic violence. In both situations, survivors may feel shame over allowing themselves to be victimized.

Language and Symptom Expression

Another influence on symptom expression is the language used by clinician and client (Diaz et al., 2009). Malgady and Constantino (1998) examined the influence of language by experimentally varying the language spoken during an assessment interview with Hispanic clinicians. They found that severity of psychopathology was found to be highest in the bilingual condition, followed by the Spanish-speaking condition, and then the English-speaking condition. There was a tendency for clinicians to rate Latino clients speaking Spanish or Spanish and English as having more severe psychopathology and as functioning less well than Latino clients speaking English only. It was not clear whether this bias was in the form of overpathologizing on the clinicians' part or whether they are more sensitive to clients' presenting symptoms when assessing in Spanish. Nevertheless, there appears to be an important effect of language on diagnosis of psychopathology.

TREATMENT ISSUES

The understanding of the role of culture, race, and ethnicity on treatment is considerably important when working with ethnic minority patients. In the following section, a discussion of how such factors can influence various domains of the treatment process (e.g., therapeutic alliance, clinical judgments, and client perspectives) is presented. It is worth noting that the following treatment considerations are not comprehensive, but rather a general overview of how acknowledging the impact

of certain cultural factors when working with ethnic minority patients can enhance the efficiency and effectiveness of treatment.

Clinician and Client Interplay

Many clients feel more comfortable discussing psychological problems with someone of the same ethnoracial background (e.g., Jackson et al., 2004), and they may answer questions about symptoms differently when ethnoracially matched (e.g., Williams & Turkheimer, 2007). Research shows that most people prefer to be matched to someone of the same ethnicity. Ethnic minority clients may perceive their counseling experience to be more effective when they are ethnoracially matched (Lee, Sutton, France, & Uhlemann, 1983), and European American clients may feel more comfortable with someone of the same ethnoracial group (Davis, Williams, & Chapman, 2011). Matching has been shown to strengthen the therapeutic alliance and improve retention (Flicker, Waldron, Turner, Brody, & Hops, 2008). However, cultural matching is not always possible due to a lack of availability of a clinician of the same ethnicity as the client, and it may not be desirable from the client's perspective (e.g., could be perceived as "forced segregation"; Pole, Gone, & Kulkarni, 2008). Furthermore, unmatched dyads provide an opportunity for expanded awareness and greater cross-cultural understanding in both the client and therapist. Thus cross-cultural training is essential for all clinicians (Williams, Tellawi, Wetterneck, & Chapman, in press).

Cultural traditions vary about the manner in which clinicians are regarded. Many consider therapists authority figures and will feel uncomfortable challenging or disagreeing with their clinician. For example, when a Japanese client enters a consulting room, it is common for the client to just sit very tensely in front of the therapist and calmly answer questions. Japanese clients typically want to perform ideally, and this is reflected in therapist-client relationship. Clients tell the therapist their issues, and then just wait for the therapist to analyze them. Clients expect the therapist to tell them what to do. From a Western viewpoint, this can be seen as dependent, but it is actually a way for Japanese people to show respect by giving power to those in authority. European American therapists can find it difficult to work with Japanese clients if the therapist is not aware of the power dynamics within the Japanese culture. When the Japanese utilize psychotherapy services, they generally apply Japanese methods of forming relationships, creating a hierarchical relationship between client and therapist. A Japanese client was assessed by a Western therapist without this understanding and the therapist believed the client had no sense of self, describing the client as passive, needy, and repressed. Japanese clients sometimes appear helpless and this might be misinterpreted as playing a victim role. However, from the client's view, it is considered culturally appropriate (Nipoda, 2002).

This example also illustrates how cultures differ in terms of what they consider to be the role of the therapist or healer. For example, within the Afrocentric framework, the essence of all things is spiritual. The spirit is energy and life force in each person, which constitutes a self-healing power. Thus, therapy becomes a process or vehicle in which individuals are helped to access their own self-healing power (Parham, 2002). This was illustrated in a recent study of male African American outpatients being treated for depression. Psychotherapy was viewed helpful only in that therapists helped clients to identify methods for improving their individual will and agency. For example,

psychotherapy may help one to express feelings, discuss consequences of one's actions, or understand why past events occurred or how past events impact reactions to current difficult life situations. The therapist was regarded as a vehicle for change rather than an agent of change (Casiano, McMickens, Williams, & Epperson, under review). Clients had learned to access their own self-healing power.

Role of Stereotypes, Biases, and the Clinician's Culture

Although most clinicians are now receiving some multicultural education in their training programs (Green, Callands, Radcliffe, Luebbe, & Klonoff, 2009), practical skills for working with members of specific minority groups are often not included. When clinicians and researchers lack the needed skills and education for effective cross-cultural interactions, they may rely on a *colorblind approach.* Colorblindness is the ideology that different ethnoracial groups should all be treated the same, without regard to cultural differences (Terwilliger, Bach, Bryan, & Williams, 2013). Minorities are often treated as if they lack characteristics that make them different from the dominant majority. Although the intent of colorblindness is to promote fairness, it often causes confusion and can paradoxically increase prejudice (e.g., Richeson & Nussbaum, 2004). When the idea of "treating everyone the same" is proposed, it is typically from the perspective of the dominant majority, implying that clients should be treated as if they were culturally European American (Terwilliger et al., 2013).

From a clinical standpoint, colorblindness could result in negative consequences for an ethnic minority client if a therapist were to suggest that the client engage in behaviors that are generally considered adaptive within European American psychological tradition but that may in fact be culturally incongruent outside of that tradition. For example, a therapist may encourage an adult client to move out of the parents' home and find his or her own apartment to assert autonomy. But in more collectivistic cultures, it may be abnormal for unmarried children to move out. Thus such an event could potentially result in a family crisis, conflict, and loss of needed emotional support. The goal, therefore, is not to treat participants as if they were European American, but as they should be treated based on the norms and customs of their particular culture. This approach, called *multiculturalism*, embraces the differences, strengths, and uniqueness of each cultural group (Terwilliger et al., 2013; Williams et al., in press).

Another issue of which clinicians must be aware concerns preconceived notions about clients based solely on ethnic group membership, or pathological stereotypes (Williams, Gooden, & Davis, 2012). These are generalizations about people used as a means of explaining and justifying differences between groups and thereby using these differences to oppress the "out-group." Social status or group position determines the content of stereotypes, and not actual personal characteristics of group members (Jost & Banaji, 1994). Groups that have fewer social and economic advantages will be stereotyped in a way that seemingly explains disparities, such as lower employment or higher illiteracy rates. Although disadvantaged group members may have greater difficulty finding a job due to in-group favoritism, discrimination, and institutional racism, the disadvantaged group member is characterized as unmotivated (could have found a job if he looked hard enough), unintelligent (not

smart enough to have that job), lazy (would rather take handouts than work), and criminal (will steal rather than work) (Williams, Gooden, & Davis, 2012).

It is important to understand that pathological stereotypes about cultural groups are unfair and inaccurate. Furthermore, all members of a society are affected by the negative social messages that espouse these stereotypes, casting disadvantaged groups in a negative light (Devine & Elliot, 1995). When we uncritically accept these negative messages, racism follows, even from professionals who mean well. This can lead to harmful, discriminatory behaviors toward clients, which may be conscious or unconscious, and overt or covert.

Perhaps the most common act of discrimination by clinicians is what is termed as the *microaggression* (Sue et al., 2007). A microaggression is a brief, everyday exchange that sends denigrating messages to a target simply because they belong to a racial minority group. Microaggressions are often unconsciously delivered in the form of slights or subtle dismissive behaviors. The target of a microaggression is often forced to ascertain whether another individual did, in fact, perpetrate a discriminatory act. This attributional ambiguity is inherently stressful and is different from an overt discriminatory act, which is more easily identified and explained. As such, the influence of racial microaggressions on stress and anxiety may lie in the uncertainty generated from such interactions (Torres et al., 2010). One study found that racial microaggressions directed against African American clients was predictive of a weaker therapeutic alliance with White therapists. This, in turn, predicted lower ratings of general competence and multicultural counseling competence, and unsurprisingly lower counseling satisfaction ratings. Racial microaggressions had a significant indirect effect on client ratings of White counselors' counseling competence through the therapeutic working alliance (Constantine, 2007).

It is important to understand that microagressions can be particularly harmful to vulnerable clients, who may already feel stigmatized and exposed even attempting therapy. Minority clients may find it difficult to respond to such remarks in counseling situations due to self-doubt and power dynamics. These problems contribute to feelings of distance from the therapist, unwillingness to disclose sensitive information, and early termination from treatment. Thus, clients may be unable to overcome the condition for which they sought help due to undesirable therapist factors. The degree of harm therapists may cause in this manner is unknown and likely underestimated (Constantine, 2007).

Culture as an Integral Part of Assessment

Americans are socialized not to acknowledge race and ethnicity, due in part to concerns of appearing biased or racist (Gaertner & Dovidio, 2005). However, this avoidance contributes to difficulty recognizing, discussing, and adapting to cultural differences (Terwilliger et al., 2013). Many European American therapists are uncomfortable discussing race in cross-racial therapeutic dyads (Knox, Burkard, Johnson, Suzuki, & Ponterotto, 2003). However, therapists actually have more success working cross-culturally when they address differences directly. Raising the issue of race early in the therapeutic relationship conveys cultural sensitivity and may address clients' concerns about a racially different counselor. When counselors communicate their own cultural background and acknowledge their client's cultural values, clients

are more likely to see their counselor as credible and feel more relaxed in therapy (Owen, Tao, Leach, & Rodolfa, 2011). Culturally competent counselors are aware of how their own cultural backgrounds and experiences influence their attitudes and values surrounding psychological processes, and this recognition enables them to better access the client's needs (Delsignore, Petrova, Harper, Stowe, Mu'Min, & Middleton, 2010).

Thus, it is important that clinicians understand culture-specific differences, which can range from amount of eye contact to specific idioms of psychological distress. Mental health professionals must make culture an integral part of each assessment as it influences patterns of communication between clinician and patient and subsequent diagnostic and treatment outcomes (Alarcón et al., 2009; Williams et al., in press). There are too many different groups for any one person to have an in-depth understanding of all, so clinicians should at least receive training specific to the ethnoracial groups most commonly served, and seek additional information and consultation when confronted with clients from completely foreign cultures.

In its ongoing effort to more widely recognize cultural context, the *DSM-5* now includes a cultural formulation interview guide designed to help clinicians assess cultural factors influencing client perspectives on their symptoms and treatment options. It includes questions about client background in terms of culture, race, ethnicity, religion, and geographical origin. The interview facilitates the process for individuals to describe distress in their own words and then relate this to how others, who may not share their culture, see their difficulties. This gives the clinician a more comprehensive basis for diagnosis and care, and may be a good starting point for those clinicians working with ethnically different clients.

Mistrust of Medical Institutions and Establishment

According to the U.S. Surgeon General, "research documents that many members of minority groups fear, or feel ill at ease, with the mental health system" (NIH, 1999). African Americans have greater distrust of the medical establishment and mental health care, many believing that medical institutions hold racist attitudes (Gamble, 1993; Whaley, 2001). Negative perceptions may be rooted in historical abuses of slaves, who were often used to test and perfect medical procedures before they were attempted on Whites (Gamble, 1997).

The most well-known example of such abuses is The Tuskegee Study of Untreated Syphilis in the African American Male. This is the longest nontherapeutic experiment on human beings in medical history. Begun in 1932 by the United States Public Health Service (USPHS), the study was designed to determine the natural course of untreated syphilis in 400 African American men in Tuskegee, Alabama. The research subjects, who had syphilis when they were enrolled in the study, were matched against 200 uninfected subjects who served as controls (Heintzelman, 2003).

The subjects were recruited with misleading promises of "special free treatment," which were actually spinal taps done without anesthesia to study the neurological effects of syphilis, and they were enrolled without informed consent. The subjects were denied antibiotic therapy when it became clear in the 1940s that penicillin was an effective treatment for the disease. On several occasions, the USPHS actually interfered to prevent subjects from obtaining treatment elsewhere (Heintzelman, 2003).

In many cases, the infected subjects passed the disease to their wives and subsequently newborn babies. Over 100 people died directly from advanced syphilis. In August 1972 an investigatory panel found the study was ethically unjustified and that penicillin should have been provided. The National Research Act, passed in 1974, mandated that all federally funded proposed research with human subjects be approved by an institutional review board (IRB). By 1992, settlement payments of approximately $40,000 were made to survivors. President Clinton publicly apologized on behalf of the federal government to the handful of study survivors in April 1997 (Heintzelman, 2003).

Many African Americans see the Tuskegee Study as representative of much current medical research even today (Freimuth et al., 2001). For instance, one study examined attitudes toward biomedical research across four ethnically diverse adult samples and found that African Americans endorsed more fear of participation in research than non-Hispanic White adults, which suggests that a cultural mistrust of research remains salient among African Americans (Katz et al., 2006). Most importantly, in cases where ethnic minorities appear hesitant or distrusting of mental health care, it is important for mental health professionals to remember the historical significance of a cultural mistrust in health care systems. Cultural knowledge of institutional abuses, combined with regular experiences of racism, maintains cultural mistrust surrounding health care.

Lack of Awareness Can Result in Misdiagnosis

Evidence shows that minorities are often misdiagnosed, due to the factors described previously. These include:

- Misuse of assessment instruments that are considered to be "gold standards."
- Diagnostic criteria based on Eurocentric observations and conceptualizations, resulting in missed or misunderstood symptoms.
- Research findings based on Eurocentric diagnostic criteria, providing less helpful information about psychopathology in non-White populations.
- Lack of adequate multicultural training for clinicians, often resulting in a problematic colorblind approach.
- Pathological stereotypes about members of specific cultural groups that affect clinician judgments.
- Poor therapeutic working alliance due to lack of cultural awareness and microaggressions against clients.

These problems are not simply academic, but result in substandard care, inappropriate treatments, and premature termination from treatment. For example, research shows that African Americans and Hispanic Americans are often overdiagnosed with psychotic disorders, and underdiagnosed with mood disorders. In particular, African Americans are more often given the diagnosis of paranoid schizophrenia than European Americans with similar symptoms (Snowden & Pingitore, 2002). This could be due in part to misinterpretation by clinicians of "healthy cultural paranoia"—a defensive posture taken by African Americans when approaching a new situation that could involve racism or discrimination (Whaley, 2001). This paranoia is not completely unfounded given the reality of discrimination and racial tensions in the

United States. Additionally, African Americans are more likely to be admitted as inpatients, even after controlling for severity of illness and demographic variables (Snowden, Hastings, & Alvidrez, 2009).

For Hispanic Americans the research results are mixed. Chui (1996) finds that Hispanics receive a diagnosis of schizophrenia less often than African Americans and non-Hispanic Whites, but they more often receive diagnoses of other mental illnesses. Solomon (1992) reports that more Puerto Ricans are diagnosed schizophrenic than any other group, including other Hispanics. This could be due to the intersection of race and ethnicity as many Puerto Ricans are both Black and Hispanic. Furthermore, when minorities are diagnosed with psychotic or affective disorders the conditions are more likely to be considered chronic, rather than acute when compared to European Americans with the same diagnoses.

Likewise, assessments of dangerousness and potential for violence are overestimated for African American inpatients, in accordance with violent and criminal stereotypes (Good, 1996; Wood, Garb, Lilienfeld, & Nezworski, 2002). One result of this bias is the overmedication of Black psychiatric patients (Wood et al., 2002). This is compounded by the fact African Americans, like many other ethnic minorities, metabolize antidepressants and antipsychotic medications more slowly than Whites and may be more sensitive to the medications. This higher sensitivity is manifested in a faster and higher rate of response and more severe side effects, including delirium when treated with doses commonly used for White patients (Munoz & Hilgenberg, 2006). Thus, African Americans may exhibit poorer medication compliance, which then may be misinterpreted as resistance to treatment.

Interestingly, Hispanic Americans are less likely to be medicated at all (Hodgkin, Volpe-Vartanian, & Alegría, 2007). Aside from limited health care access among Latino populations (Perez-Escamilla, 2010), another potential explanation could be a lack of adherence to medication throughout the course of mental illness (Hodgkin et al., 2007; Colby, Wang, Chhabra, & Pérez-Escamilla, 2012). In particular, Hodgkin and colleagues (2007) utilized data from the National Latino and Asian American Study (NLAAS) and found that 18.9% of Hispanic Americans who discontinued antidepressant medication decided to do so without consulting a health professional. Researchers noted that possessing English-language proficiency, older age, being married, having insurance, and consistent visits to see a therapist were related to better antidepressant adherence in this sample.

African Americans are diagnosed less accurately than European Americans when they are suffering from depression and seen in primary care (Borowsky et al., 2000), or when they are seen for psychiatric evaluation in an emergency room (Strakowski et al., 1997). One study found that African Americans were less likely than Whites to receive an antidepressant when their depression was first diagnosed (27% versus 44%), and among those who did receive antidepressant medications, African Americans were less likely to receive the newer SSRI medications than were the White patients (Melfi, Croghan, & Hanna, 2000).

In terms of substance abuse, 15% of the general population will abuse a substance in their lifetime and 4% will abuse a substance within 12 months (Kessler et al., 2005a; Kessler et al., 2005b). Negative social stereotypes dictate that drug users are largely Black and Hispanic. Most people are surprised to learn that African American youth are significantly less likely to use tobacco, alcohol, or drugs than European Americans

or Hispanic Americans (Centers for Disease Control, 2000). In fact, African Americans spend 25% less than Whites on alcohol (U.S. Department of Labor, 2002). The National Longitudinal Alcohol Epidemiological Survey indicated that Whites were more likely to use drugs over their lifetime but Blacks were more dependent than Whites, underscoring differential access to effective treatments (Grant, 1996). Blacks and Whites tend to abuse different drugs (e.g., crack versus cocaine), and the drugs used by African Americans carry harsher penalties and are more likely to be the targets of law enforcement efforts (e.g., Beckett, Nyrop, & Pfingst, 2006). Thus, institutionalized racism may play a role in drug abuse outcomes and access to treatment.

CONCLUSIONS

This chapter represents a charge to mental health professionals to fully consider and subsequently integrate racial, ethnic, and cultural variables into inevitable work with ethnic minority individuals. The importance of such integration undoubtedly has a profound impact on several areas including but not limited to the following: assessment, expression of psychopathology, diagnostic practices, mental health disparities, treatment outcome studies, continued dearth of ethnic minorities involved in research studies, and a continued paucity of researchers and practitioners of color. Explicit acknowledgment of inherent biases that we all possess in addition to understanding the importance of incorporating cultural variables throughout *all* portions of our work with ethnic minority populations are important first steps to decreasing mental health disparities. Additionally, we continue to underscore the importance of reviewing the empirical literature as it pertains to ethnic minority populations since "all measures are *not* created equal." Moreover, there continues to be a disconnect between much of our scientific training with regard to making decisions about assessment measures, how psychopathology is expressed in many ethnic minority individuals, which often deviates from "traditional" expressions, and our subsequent implementation of treatment.

Although significant strides have been made in the more recent empirical literature endemic to ethnic minority individuals, we as mental health professionals have to be increasingly cognizant of integrating identified cultural factors throughout all facets of both our own work and in training the next generation. Ethnoracial minorities are currently 36.6% of the U.S. population, and 50.4% of all births (U.S. Census Bureau, 2011, 2012), with non-Hispanic Whites projected to be a minority in the United States by 2050 (Nagayama Hall, 2001). Thus, much of the work that we have highlighted is vitally important to our cultural competence in the 21st century.

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PART II

SPECIFIC DISORDERS

CHAPTER 5

Schizophrenia

DENNIS R. COMBS, KIM T. MUESER, and EMILY DRAKE

INTRODUCTION

Schizophrenia is the most debilitating and costly of all adult psychiatric illnesses. Despite the recent trend toward community-oriented treatment, about 25% of all psychiatric hospital beds are occupied by persons with schizophrenia. The costs of treating schizophrenia are significant in terms of both financial and personal costs. It was estimated that the fiscal cost of schizophrenia in the United States was $62.7 billion in 2002 (Wu et al., 2005) and $6.85 billion in Canada in 2004 (Goeree et al., 2005). About one-third (roughly 22.7 billion) of the U.S. dollars spent on schizophrenia is directed to the treatment and medical needs of this population. Despite the economic costs, the impact on the person's social and occupational functioning over a lifetime may be even more devastating (Knapp, Mangalore, & Simon, 2004). In fact, the largest indirect cost associated with schizophrenia is the loss of productivity over the lifetime. The burden of schizophrenia places the disorder as one of the top 10 most disabling conditions in the world in terms of illness-adjusted life years (Mueser & McGurk, 2004; Murray & Lopez, 1996). Even when persons with schizophrenia receive optimal treatments, many continue to experience substantial impairments throughout most of their lives.

Since schizophrenia was first described more than 100 years ago, the nature of the disorder has been hotly debated, and public misconceptions about it have been commonplace. In recent years, there has been a growing consensus among clinicians and researchers to more rigorously define the psychopathology and diagnostic features of this disorder. Once referred to as a "wastebasket diagnosis, " the term *schizophrenia* is now used to describe a specific clinical syndrome. Current arguments about the disorder have focused on the validity of the diagnostic category of schizophrenia, and alternative models argue that it is more beneficial to focus on psychotic symptoms (e.g., paranoia, hallucinations, and delusions) (Bentall, Jackson, & Pilgrim, 1988). Nonetheless, an understanding of the core clinical features of schizophrenia is necessary for diagnosis and treatment planning. After many years of struggling to improve the long-term course of schizophrenia, there is now abundant evidence that combined pharmacological and psychosocial interventions can have a major impact on improving functioning. This chapter provides an up-to-date review

of schizophrenia, with a particular focus on the psychopathology of the illness and its impact on other domains of functioning.

DESCRIPTION OF THE DISORDER

Schizophrenia is characterized by impairments in social functioning, including difficulty establishing and maintaining interpersonal relationships, problems working or fulfilling other instrumental roles (e.g., student, homemaker, employee), and difficulties caring for oneself (e.g., poor grooming and hygiene). These problems in daily living, in the absence of significant impairment in intellectual functioning, are the most distinguishing characteristics of schizophrenia and are a necessary criterion for its diagnosis according to most diagnostic systems (e.g., American Psychiatric Association [APA], 2013). Consequently, many individuals with the illness depend on others to meet their daily living needs. For example, estimates suggest that between 25% and 60% of persons with schizophrenia live with relatives, and an even higher percentage rely on relatives for caregiving (Goldman, 1982; Torrey, 2001). Time spent providing support and care for a person with schizophrenia can be substantial (with reports as high as 6 to 9 hours per day for some families; Magliano et al., 1998). It appears that the emotional and physical burden on caregivers is found across cultures (Breitborde, Lopez, Chang, Kopelowicz, & Zarate, 2009; Huang, Hung, Sun, Lin, & Chen, 2009; Zahid & Ohaeri, 2010). Individuals without family support typically rely on mental health, residential, and case management services to get their basic needs met. In the worst-case scenario, persons with schizophrenia who have insufficient contact with relatives and who fall between the cracks of the social service delivery system end up in jail (Torrey et al., 1992) or become homeless, with between 10% and 20% of homeless persons having schizophrenia (Susser, Stuening, & Conover, 1989).

In addition to the problems of daily living that characterize schizophrenia, individuals with the illness experience a range of different symptoms. The most common symptoms include positive symptoms (e.g., hallucinations, delusions, disorganization), negative symptoms (e.g., social withdrawal, apathy, anhedonia, poverty of speech), cognitive impairments (e.g., memory difficulties, planning ability, abstract thinking), and problems with mood (e.g., depression, anxiety, anger). The specific nature of these symptoms is described in greater detail in the following section. The symptoms of schizophrenia appear to account for some, but not all, of the problems in social functioning (Glynn, 1998).

The various impairments associated with schizophrenia tend to be long term, punctuated by fluctuations in severity (i.e., relapse) over time. For this reason, schizophrenia has a broad impact on the family, and individuals are often impeded from pursuing personal life goals. Despite the severity of the disorder, advances in the treatment of schizophrenia provide solid hope for improving the outcome.

CLINICAL PICTURE

Most studies on the dimensions of schizophrenia agree on at least three major groups of symptoms (Liddle, 1987; Mueser, Curran, & McHugo, 1997; Van Der Does, Dingemans, Linszen, Nugter, & Scholte, 1993), including positive symptoms, negative symptoms, and cognitive impairments. Positive symptoms refer to thoughts, sensory

experiences, and behaviors that are present in persons with the disorder but are ordinarily absent in persons without the illness. Common examples of positive symptoms include hallucinations (e.g., hearing voices, seeing visions), delusions (e.g., believing that others are persecuting the person), and bizarre, disorganized behavior (e.g., maintaining a peculiar posture for no apparent reason, wearing multiple layers of clothes). Persecutory delusions (i.e., belief that some entity, group, or person has clear ongoing or future intentions to harm the person) are the most common type of delusion found in schizophrenia (Appelbaum, Robbins, & Roth, 1999; as reviewed in Bentall, Corcoran, Howard, Blackwood, & Kinderman, 2001). About 75% of persons with schizophrenia report hallucinations (Cutting, 1995). Auditory hallucinations are the most common form and are frequently derogatory, negative, or abusive, although some can be benevolent, comforting, and kind (Chadwick & Birchwood, 1995; Copolov, Mackinnon, & Trauer, 2004; Cutting, 1995). Less frequent, but more specific to schizophrenia, are voices that keep a running commentary on the person's actions or consist of two or more voices having a conversation. Auditory hallucinations can range from inaudible sounds (buzzing sounds, noises, muffled speech) or clearly perceived voices of either gender and can occur intermittently or on a continuous basis. It has been assumed that visual hallucinations were infrequent in schizophrenia and were more reflective of a medical condition (prevalence of 10% to 15% in schizophrenia), but recent evidence suggests that these symptoms are more common than initially believed, especially in more severe forms of the disorder (Bracha, Wolkowitz, Lohr, Karson, & Bigelow, 1989; Mueser, Bellack, & Brady, 1990).

Negative symptoms, conversely, refer to the absence or diminution of cognitions, feelings, or behaviors that are ordinarily present in persons without the illness. Common negative symptoms include blunted or flattened affect (e.g., diminished facial expressiveness), poverty of speech (i.e., diminished verbal communication), anhedonia (i.e., inability to experience pleasure), apathy, psychomotor retardation (e.g., slow rate of speech), and physical inertia. The positive symptoms of schizophrenia tend to fluctuate over the course of the disorder and are often in remission between episodes of the illness. In addition, positive symptoms tend to be responsive to the effects of antipsychotic medication (Kane & Marder, 1993). In contrast, negative symptoms and cognitive impairments tend to be stable over time and are less responsive to antipsychotic medications (Greden & Tandon, 1991). However, there is some evidence that atypical antipsychotic medications, such as clozapine, risperidone, and olanzapine, have a beneficial impact on negative symptoms and cognitive functioning (Breier, 2005; Green et al., 1997; Tollefson & Sanger, 1997; Wahlbeck, Cheine, Essali, & Adams, 1999).

Aside from the core symptoms of schizophrenia, many persons with schizophrenia experience negative emotions (e.g., depression, anxiety, and anger) as a consequence of their illness (Freeman & Garety, 2003). Depression is quite common (estimated comorbidity rate of 45%; Leff, Tress, & Edwards, 1988) among people with schizophrenia and has been associated with poor outcomes (e.g., increased hospital use, lower employment rates) and suicidal tendencies (Sands & Harrow, 1999). Depressive symptoms can occur during all phases of the illness (prepsychotic, prodrome, acute, and remission), but they tend to attenuate as the active psychotic symptoms remit (Birchwood, Iqbal, Chadwick, & Trower, 2000). In addition, it was generally estimated that approximately 10% of the persons with this illness die from suicide (Bromet, Naz,

Fochtmann, Carlson, & Tanenberg-Karant, 2005; Drake, Gates, Whitaker, & Cotton, 1985; Jobe & Harrow, 2005; Roy, 1986), but recent research examining suicide rates has lowered this estimate to around 4.0% to 5.6% (Inskip, Harris, & Barraclough, 1998; Palmer, Pankratz, & Bostwick, 2005). Risk of suicide is greater in the presence of mood symptoms and substance use, if previous suicide attempts were made, during the initial onset of the disorder (Hawton, Sutton, Haw, Sinclair, & Deeks, 2005; first psychotic episode; rates 11% to 26%, as reviewed in Malla & Payne, 2005), and in time immediately preceding and following inpatient hospitalization (Qin & Nordentoft, 2005). Anxiety is also common in schizophrenia (estimated comorbidity rate of 43%) and is a frequent precursor to psychosis (Argyle, 1990; Braga, Mendlowicz, Marrocos, & Figueria, 2005; Cosoff & Hafner, 1998; Penn, Hope, Spaulding, & Kucera, 1994; Tien & Eaton, 1992). Specifically, there is evidence for the role of anxiety in both the formation and maintenance of persecutory delusions (threat beliefs) as well as hallucinations (Freeman et al., 2002; Freeman & Garety, 2003). Finally, anger, hostility, and social avoidance may also be present, especially when the person is paranoid (Bartels, Drake, Wallach, & Freeman, 1991; Freeman, Garety, & Kuipers, 2001; Gay & Combs, 2005). Interestingly, as paranoia increases, so does the tendency to perceive ambiguous interactions in a negative, threatening manner (Combs & Penn, 2004; Freeman et al., 2005).

In addition to the positive symptoms and negative emotions commonly present in schizophrenia, individuals with this diagnosis often have comorbid substance use disorders. Epidemiological surveys have repeatedly found that persons with psychiatric disorders are at increased risk for alcohol and drug abuse (Mueser et al., 1990; Mueser, Yarnold, & Bellack, 1992). This risk is highest for persons with the most severe psychiatric disorders, including schizophrenia and bipolar disorder. For example, individuals with schizophrenia are more than 4 times as likely to have a substance abuse disorder as are individuals in the general population (Regier et al., 1990). In general, approximately 50% of all persons with schizophrenia have a lifetime history of substance use disorder, and 25% to 35% have a recent history of such a disorder (Mueser, Bennett, & Kushner, 1995). The presence of comorbid substance use disorders in schizophrenia has consistently been found to be associated with a worse course of the illness, including increased vulnerability to relapses and hospitalizations, housing instability and homelessness, violence, economic family burden, and treatment noncompliance (Drake & Brunette, 1998). For these reasons, the recognition and treatment of substance use disorders in persons with schizophrenia is crucial to the overall management of the illness.

Another important clinical feature of schizophrenia is lack of insight and compliance with treatment (Amador & Gorman, 1998; Amador, Strauss, Yale, & Gorman, 1991). Many individuals with schizophrenia have little or no insight into the fact that they have a psychiatric illness or even that they have any problems at all. This denial of illness can lead to noncompliance with recommended treatments, such as psychotropic medications and psychosocial therapies (McEvoy et al., 1989). Furthermore, fostering insight into the illness is a difficult and often impossible task with these persons.

Noncompliance with treatment is a related problem, but it can also occur because of the severe negativity often present in the illness, independent of poor insight. Problems with paranoia and distrust may contribute to noncompliance, in that

some persons may believe medications or treatment providers are dangerous to them. Furthermore, the side effects of some medications (e.g., sedation, dry mouth, motor side effects), particularly the conventional antipsychotics, are unpleasant and can also lead to noncompliance. Medication noncompliance increases the risk of relapse, and between 50% and 75% of individuals who discontinue their medication will relapse within 1 year. Therefore, treatment compliance is a major concern to clinical treatment providers (Buchanan, 1992). It has been argued that the newer atypical antipsychotics may lead to higher rates of compliance owing to better side effect profiles (Breier, 2005). However, a recent study of 63,000 individuals with schizophrenia in the Veteran's Affairs medical system found widespread noncompliance (compliance measured in terms of filling needed prescriptions) across both conventional and atypical antipsychotics (Valenstein et al., 2004). Strategies for enhancing compliance involve helping the person become a more active participant in his or her treatment, identifying personal goals of treatment that have high relevance for that individual, and helping the person to develop strategies for taking medications into the daily routines (Azrin & Teichner, 1998; Corrigan, Liberman, & Engle, 1990; Kemp, Hayward, Applewhaite, Everitt, & David, 1996; Kemp, Kirov, Everitt, Hayward, & David, 1998).

People with schizophrenia are sometimes assumed to be violent or otherwise dangerous. Indeed, rates of violence have been found to be relatively higher in people with schizophrenia and other severe mental illnesses compared to the general population (Hodgins, Mednick, Brennan, Schulsinger, & Engberg, 1996; Swanson, Holzer, Ganju, & Jono, 1990). However, a more accurate comparison may be to examine the rates of violence between schizophrenia and other psychiatric disorders. Data from the MacArthur Risk Assessment Study found that the actual rates of violence for persons with schizophrenia was 8% for the first 20 weeks following discharge (most violent events occur in the first 20 weeks) and 14% over the course of a 1-year period (Monahan et al., 2001). In comparison, the rates of violence for persons with schizophrenia were actually lower than those for persons with depression and bipolar disorder for the same time period. A prospective study of violent behaviors in females with severe mental illness reported a prevalence rate of 17% over a 2-year period (Dean et al., 2006). Rates vary widely depending upon source of information (e.g., self-report vs. collateral reports), definition of violence, population studied (e.g., inpatients versus outpatients), and where the research takes place (e.g., country). However, it should be emphasized that the majority of people with schizophrenia and other mental illnesses are not violent (Swanson, 1994). When violence does occur, it is often associated with substance abuse (Steadman et al., 1998) or the combination of substance abuse and medication noncompliance (Swartz et al., 1998). Other factors such as psychopathy (Nolan, Volavka, Mohr, & Czobor, 1999) or antisocial personality disorder (Hodgins & Côté, 1993, 1996) also have been implicated. Finally, targets of violence tend to be family members or friends rather than strangers, which is not unexpected given that most persons with schizophrenia rely heavily on family members for support (Steadman et al., 1998).

Although there is an increased rate of violence in schizophrenia, people with schizophrenia are much more likely to be the victims of violence and violent crime (Hiday, Swartz, Swanson, Borum, & Wagner, 1999). About 34% to 53% of individuals with severe mental illness report childhood sexual or physical abuse (Greenfield,

Strakowski, Tohen, Batson, & Kolbrener, 1994; Jacobson & Herald, 1990; Rose, Peabody, & Stratigeas, 1991; Ross, Anderson, & Clark, 1994), and 43% to 81% report some type of victimization over their lives (Carmen, Rieker, & Mills, 1984; Hutchings & Dutton, 1993; Jacobson, 1989; Jacobson & Richardson, 1987; Lipschitz et al., 1996). Two recent surveys of a large number of people with severe mental illness found high rates of severe physical or sexual assault in the past year (Goodman et al., 2001; Silver, Arseneault, Langley, Caspi, & Moffitt, 2005). These numbers are striking compared to estimates of the general population, in which 0.3% of women and 3.5% of men reported assault in the past year (Tjaden & Thoennes, 1998). Studies of the prevalence of interpersonal trauma in women with severe mental illness indicate especially high vulnerability to victimization, with rates ranging as high as 77% to 97% for episodically homeless women (Davies-Netzley, Hurlburt, & Hough, 1996; Goodman, Dutton, & Harris, 1995).

The prevalence of posttraumatic stress disorder (PTSD) among people with schizophrenia and other severe mental illnesses in various samples has ranged from 14% to 43% (Cascardi, Mueser, DeGirolomo, & Murrin, 1996; Craine, Henson, Colliver, & MacLean, 1988; Grubaugh, Zinzow, Paul, Egede, & Frueh, 2011; Mueser, Bond, Drake, & Resnick, 1998; Mueser et al., 2004; Switzer et al., 1999), but has been as low as 3.8% (Braga et al., 2005). These current rates of PTSD are far in excess of the lifetime prevalence of PTSD in the general population, with estimates ranging between 8% and 12% (Breslau, Davis, Andreski, & Peterson, 1991; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; Resnick, Kilpatrick, Dansky, Saunders, & Best, 1993). Thus, interpersonal violence is so common in the serious mental illness population that it must sadly be considered a normative experience (Goodman, Dutton, & Harris, 1997).

DIAGNOSTIC CONSIDERATIONS

The diagnostic criteria for schizophrenia are fairly similar across a variety of different diagnostic systems. In general, the diagnostic criteria specify some degree of work, social, or self-care impairment, combined with positive and negative symptoms lasting a significant duration (e.g., 6 months or more). The diagnostic criteria for schizophrenia according to *DSM-V* (APA, 2013) must include the presence of two or more of the following five symptoms: delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, or negative symptoms. One of the symptoms must be delusions, hallucinations, or disorganized speech. The symptoms must have been present at least for a month, unless successfully treated. Since the disorder's onset, the symptoms must be accompanied by a decrease in functioning such as work or social interaction, or self-care must be below the level that existed prior to the disorder's onset. Also, for a diagnosis of schizophrenia, there must be continuous signs of the disturbance for at least 6 months.

The diagnosis of schizophrenia requires a clinical interview with the patient, a thorough review of all available records, and standard medical evaluations to rule out the possible role of organic factors (e.g., CAT scan to rule out a brain tumor). In addition, because many persons with schizophrenia are poor historians or may not provide accurate accounts of their behavior, information from significant others, such as family members, is often critical to establish a diagnosis of schizophrenia. The use of family and other informants is especially important in the assessment of prodromal

and prepsychotic states. Because of the wide variety of symptoms characteristic of schizophrenia and variations in interviewing style and format across different clinical interviewers, the use of structured clinical interviews, such as the Structured Clinical Interview for *DSM* (SCID; First, Spitzer, Gibbon, & Williams, 1996) can greatly enhance the reliability and validity of psychiatric diagnosis.

Structured clinical interviews have two main advantages over more open clinical interviews. First, structured interviews provide definitions of the key symptoms, agreed upon by experts, thus making explicit the specific symptoms required for diagnosis. Second, by conducting the interview in a standardized format, including a specific sequence of asking questions, variations in interviewing style are minimized, thus enhancing the comparability of diagnostic assessments across different clinicians. The second point is especially crucial considering that most research studies of schizophrenia employ structured interviews to establish diagnoses. It is important that interviewers are properly trained and interrater reliability with a criterion-trained or expert rater is established before the use of structured interviews are initiated. If the findings of clinical research studies are to be generalized into clinical practice, efforts must be taken to ensure the comparability of the patient populations and the assessment techniques employed.

The symptoms of schizophrenia overlap with many other psychiatric disorders. Establishing a diagnosis of schizophrenia requires particularly close consideration of four other overlapping disorders: substance use disorders, affective disorders, schizoaffective disorder, and delusional disorder. We discuss issues related to each of these disorders and the diagnosis of schizophrenia in the following sections.

Substance Use Disorders

Substance use disorder, such as alcohol dependence or drug abuse, can either be a differential diagnosis to schizophrenia or a comorbid disorder (i.e., the individual can have both schizophrenia and a substance use disorder). With respect to differential diagnosis, substance use disorders can interfere with a clinician's ability to diagnosis schizophrenia and can lead to misdiagnosis if the substance abuse is covert, denied, or not reported accurately (Corty, Lehman, & Myers, 1993; Kranzler et al., 1995). Psychoactive substances, such as alcohol, marijuana, cocaine, and amphetamines, can produce symptoms that mimic those found in schizophrenia, such as hallucinations, delusions, and social withdrawal (Schuckit, 1995). In those cases in which the substance is involved in the etiology of psychosis, a diagnosis of substance-induced psychotic disorder would be appropriate. Further complicating matters, the use of these substances can exacerbate psychotic symptoms and in many cases lead to a return of acute psychosis.

Because the diagnosis of schizophrenia requires the presence of specific symptoms in the absence of identifiable organic factors, schizophrenia can only be diagnosed in persons with a history of substance use disorder by examining the individual's functioning during sustained periods of abstinence from drugs or alcohol. When such periods of abstinence can be identified, a reliable diagnosis of schizophrenia can be made. However, persons with schizophrenia who have a long history of substance abuse, with few or no periods of abstinence, are more difficult to assess. For example, in a sample of 461 individuals admitted to a psychiatric hospital, a psychiatric

diagnosis could be neither confirmed nor ruled out because of history of substance abuse in 71 persons (15%; Lehman, Myers, Dixon, & Johnson, 1994).

Substance use disorder is the most common comorbid diagnosis for persons with schizophrenia. Because substance abuse can worsen the course and outcome of schizophrenia, recognition and treatment of substance abuse in schizophrenia is a critical goal of treatment. The diagnosis of substance abuse in schizophrenia is complicated by several factors. Substance abuse, as in the general population, is often denied because of social and legal sanctions (Galletly, Field, & Prior, 1993; Stone, Greenstein, Gamble, & McLellan, 1993), a problem that may be worsened in this population because of a fear of losing benefits. Denial of problems associated with substance abuse, a core feature of primary substance use disorders, may be further heightened by psychotic distortions and cognitive impairments present in schizophrenia. Furthermore, the criteria used to establish a substance use disorder in the general population are less useful for diagnosis in schizophrenia (Corse, Hirschinger, & Zanis, 1995). For example, the common consequences of substance abuse in the general population of loss of employment, driving under the influence of alcohol, and relationship problems are less often experienced by people with schizophrenia, who are often unemployed, do not own cars, and have limited interpersonal relationships. Rather, persons with schizophrenia more often experience increased symptoms and rehospitalizations, legal problems, and housing instability because of substance abuse (Drake & Brunette, 1998).

Individuals with schizophrenia tend to use smaller quantities of drugs and alcohol (Cohen & Klein, 1970; Crowley, Chesluk, Dilts, & Hart, 1974; Lehman et al., 1994) and rarely develop the full physical dependence syndrome that is often present in persons with a primary substance use disorder (Corse et al., 1995; Drake et al., 1990; Test, Wallisch, Allness, & Ripp, 1989) or show other physical consequences of alcohol such as stigmata (Mueser et al., 1999). Even very low scores on instruments developed for the primary substance use disorder population, such as the Addiction Severity Inventory, may be indicative of substance use disorder in persons with schizophrenia (Appleby, Dyson, Altman, & Luchins, 1997; Corse et al., 1995; Lehman, Myers, Dixon, & Johnson, 1996). Because of the difficulties in using existing measures of substance abuse for people with schizophrenia and other severe mental illnesses, a screening tool was developed specifically for these populations: the Dartmouth Assessment of Lifestyle Instrument (DALI; Rosenberg et al., 1998). The DALI is an 18-item questionnaire that has high classification accuracy for current substance use disorders of alcohol, cannabis, and cocaine for people with severe mental illness.

Despite the difficulties involved in assessing comorbid substance abuse in persons with schizophrenia, recent developments in this area indicate that if appropriate steps are taken, reliable diagnoses can be made (Drake, Rosenberg, & Mueser, 1996; Maisto, Carey, Carey, Gordon, & Gleason, 2000). The most critical recommendations for diagnosing substance abuse in schizophrenia include (a) maintain a high index of suspicion of current substance abuse, especially if a person has a past history of substance abuse; (b) use multiple assessment techniques, including self-report instruments, interviews, clinician reports, reports of significant others, and biological assays for the presence of substances, which are routinely collected on admission to inpatient treatment; and (c) be alert to signs that may be subtle indicators of the presence of a substance use disorder, such as unexplained symptom relapses, familial conflict,

money management problems, and sudden depression or suicidality. Once a substance use disorder has been diagnosed, integrated treatment that addresses both the schizophrenia and the substance use disorder (co-occurring disorders) is necessary to achieve a favorable clinical outcome (Drake, Mercer-McFadden, Mueser, McHugo, & Bond, 1998).

Mood Disorders

Schizophrenia overlaps more prominently with the major mood disorders than any other psychiatric disorder. The differential diagnosis of schizophrenia from mood disorders is critical, because the disorders respond to different treatments, particularly pharmacological interventions. Two different mood disorders can be especially difficult to distinguish from schizophrenia: bipolar disorder with psychotic features and major depression. The differential diagnosis of these disorders from schizophrenia is complicated by the fact that mood symptoms are frequently present in all phases of schizophrenia (prodrome, acute, and remission), and psychotic symptoms (e.g., hallucinations, delusions) may be present in persons with severe mood disorders (APA, 2013; Pope & Lipinski, 1978).

The crux of making a differential diagnosis between schizophrenia and a major mood disorder is determining whether psychotic symptoms are present in the absence of mood symptoms. If there is strong evidence that psychotic symptoms persist even when the person is not experiencing symptoms of mania or depression, then the diagnosis is either schizophrenia or the closely related disorder of schizoaffective disorder (discussed in the following section). If, on the other hand, symptoms of psychosis are present only during a mood episode, but disappear when the person's mood is stable, then the appropriate diagnosis is either major depression or bipolar disorder. For example, it is common for people with bipolar disorder to have hallucinations and delusions during the height of a manic episode, but for these psychotic symptoms to remit when the person's mood becomes stable again. Similarly, persons with major depression often experience hallucinations or delusions during a severe depressive episode, which subside as their mood improves. If the patient experiences chronic mood problems, meeting criteria for manic, depressive, or mixed episodes, it may be difficult or impossible to establish a diagnosis of schizophrenia, because there are no sustained periods of stable mood.

Schizoaffective Disorder

Schizoaffective disorder is a diagnostic entity that overlaps with both the mood disorders and schizophrenia (APA, 2013). Three conditions must be met for a person to be diagnosed with schizoaffective disorder: (1) the person must meet criteria for a major mood episode (depressive or manic mood episodes) along with symptoms from criterion A from schizophrenia; (2) the person has delusions or hallucinations for 2 or more weeks in the absence of a major mood episode; and (3) the mood symptoms have to be present for a majority of the illness's duration (i.e., a person who experiences brief, transient mood states and who is chronically psychotic and has other long-standing impairments would be diagnosed with schizophrenia, rather than schizoaffective disorder).

Schizoaffective disorder and major mood disorder are frequently mistaken for one another because it is incorrectly assumed that schizoaffective disorder simply requires the presence of both psychotic and mood symptoms at the same time. Rather, as described in the preceding section, if psychotic symptoms always coincide with mood symptoms, the person has a mood disorder, whereas if psychotic symptoms are present in the absence of a mood episode, the person meets criteria for either schizoaffective disorder or schizophrenia. Thus, schizoaffective disorder requires longitudinal information about the relationship between mood and psychosis to make a diagnosis. This information is often obtained from the individual but is subject to memory and self-reporting biases (poor insight, or lack of awareness of mood states). The distinction between schizophrenia and schizoaffective disorder can be more difficult to make, because judgment must be made as to whether the affective symptoms have been present for a substantial part of the person's illness. Decision rules for determining the extent to which mood symptoms must be present to diagnose a schizoaffective disorder have not been clearly established.

Although the differential diagnosis between schizophrenia and schizoaffective disorder is difficult to make, the clinical implications of this distinction are less important than between the mood disorders and either schizophrenia or schizoaffective disorder. Research on family history and treatment response suggest that schizophrenia and schizoaffective disorder are similar disorders and respond to the same interventions (Kramer et al., 1989; Levinson & Levitt, 1987; Levinson & Mowry, 1991; Mattes & Nayak, 1984). In fact, many studies of schizophrenia routinely include persons with schizoaffective disorder and find few differences. Therefore, the information provided in this chapter on schizophrenia also pertains to schizoaffective disorder, and the differential diagnosis between the two disorders is not of major importance from a clinical perspective.

DELUSIONAL DISORDER

Delusions can be found in schizophrenia, schizoaffective disorder, severe mood disorders, organic conditions, and delusional disorder and are a nonspecific symptom in many cases. Persons with delusional disorder develop fixed delusions and do not show the other symptoms of schizophrenia (prominent auditory hallucinations, disorganization, odd or bizarre behaviors, negative symptoms). The delusion may lead to problems with others, but in general the person has good social, educational, and occupational functioning. Tactile and olfactory hallucinations can be present and will usually be incorporated into the delusional belief. Delusional disorder is more common in females (3:1 female-to-male ratio) and has a later age of onset (mean age of 40; Evans, Paulsen, Harris, Heaton, & Jeste, 1996; Manschreck, 1996; Yamada, Nakajima, & Noguchi, 1998). Delusional disorder accounts for 1% to 4% of all inpatient admissions and is relatively rare in clinical practice (Kendler, 1982).

In previous editions of the *DSM*, the differential diagnosis between delusional disorder and schizophrenia is based on the presence of nonbizarre delusions and absence of other symptoms of schizophrenia. Nonbizarre delusions are based on events or situations that could occur in real life but are highly improbable and lack supporting evidence (Sedler, 1995). Examples of nonbizarre delusions include being watched, followed, spied upon, harassed, loved, or poisoned. In contrast, bizarre

delusions involve mechanisms not believed to exist in an individual's culture, such as beliefs of thought insertion, control, and broadcasting. In reality, the distinction between nonbizarre and bizarre beliefs is highly subjective and difficult (Junginger, Barker, & Coe, 1992; Sammons, 2005). However, in the *DSM-5* the issue of nonbizarre versus bizarre delusions has been removed and it emphasizes the presence of fixed delusions of any type that are present for 1 month. Many persons with delusions will provide convincing arguments that their beliefs are true, and a decision on whether the belief is plausible must often be made with very little corroborating evidence (Flaum, Arndt, & Andreasen, 1991; Jones, 1999). An examination of the person's history, premorbid and current functioning, and symptom profile can be useful in distinguishing delusional disorder from schizophrenia. A structured interview, such as the SCID, can be useful in assessing delusional beliefs along with the other symptoms of schizophrenia.

EPIDEMIOLOGY

It is estimated that approximately 2.2 million persons in the United States have schizophrenia at any given time (Narrow, Rae, Robins, & Regier, 2002; Torrey, 2001). It is believed that 51 million persons have schizophrenia worldwide. The annual incidence of new cases of schizophrenia ranges from 8 to 40 per 100,000 persons (Jablensky, 2000; McGrath et al., 2004, as cited in Tandon, Kesavan, & Nasrallah, 2008a). Point prevalence for any given time period ranges between 3% and 7% per 1,000 persons, with some estimates as high as 10% (Goldner, Hsu, Waraich, & Somers, 2002; Jablensky, 2000; Saha, Chant, Welham, & McGrath, 2005). The lifetime risk for developing schizophrenia appears to be about 0.7% on average (see Saha et al., 2005, as reviewed in Tandon et al., 2008a).

In general, the prevalence of schizophrenia is believed to be remarkably stable across a wide range of different populations and cultures (Crow, 2008; Saha, Welham, Chant, & McGrath, 2006; Tandon et al., 2008a). There has been little difference in the rates of schizophrenia according to gender, race, religion, or level of industrialization (Jablensky, 1999). Similar incidence rates and symptom patterns were found across 10 countries in a study sponsored by the World Health Organization (WHO; Jablensky et al., 1992). However, a more recent review of prevalence studies showed considerable heterogeneity in the rates of schizophrenia among different countries that may be partly owing to variations in diagnostic criteria (Goldner et al., 2002). Furthermore, there is evidence that schizophrenia is more heavily concentrated in urban areas of industrialized countries and, in fact, persons from developing countries may have a better prognosis and course of illness (Jablensky, 2000; Jablensky et al., 2000; Peen & Dekker, 1997; Takei, Sham, O'Callaghan, Glover, & Murray, 1995; Torrey, Bowler, & Clark, 1997). This increased risk appears to be related not only to the likelihood of people with schizophrenia drifting to urban areas, but to being born in urban areas as well, which suggests that "urbanicity" has an effect on schizophrenia (Torrey et al., 1997).

Because schizophrenia frequently has an onset during early adulthood when important educational, social, and occupational milestones are often achieved, persons with the illness are especially affected in that they are less likely to marry or remain married, particularly males (Eaton, 1975; Munk-Jørgensen, 1987), and they are

less likely to complete higher levels of education (Kessler, Foster, Saunders, & Stang, 1995) and have problems in occupational performance (Marwaha & Johnson, 2004). In terms of employment rates, only 14% to 20% of persons with schizophrenia hold competitive employment despite reporting a desire to work (Mueser, Salyers, & Mueser, 2001; Rosenheck et al., 2006). It has long been known that there is an association between poverty and schizophrenia, with people belonging to lower socioeconomic classes more likely to develop the disorder (Hollingshead & Redlich, 1958; Salokangas, 1978).

Historically, two theories have been advanced to account for this association. The social drift hypothesis postulates that the debilitating effects of schizophrenia on capacity to work result in a lowering of socioeconomic means, and hence poverty (Aro, Aro, & Keskimäki, 1995). The environmental stress hypothesis proposes that the high levels of stress associated with poverty precipitate schizophrenia in some individuals who would not otherwise develop the illness (Bruce, Takeuchi, & Leaf, 1991). Recently, attention has been aimed at different ethnic and migratory groups, such as second-generation Afro-Caribbeans living in the United Kingdom, who show higher incidence rates of schizophrenia (Boydell et al., 2001; Cantor-Graae & Selten, 2005).

It is believed that being a minority in a potentially hostile social environment where racism and discrimination are present may lead to increased stress and potentially higher rates of symptoms (Clark, Anderson, Clark, & Williams, 1999; Combs et al., 2006). Both of these explanations may be partly true, and longitudinal research on changes in socioeconomic class status (SES) and schizophrenia provide conflicting results. For example, Fox (1990) reanalyzed data from several longitudinal studies and found that after controlling for initial levels of socioeconomic class, downward drift was not evident. Furthermore, Samele et al. (2001) found that a downward drift in occupational functioning over a 2-year period was not linked to illness course or prognosis. However, Dohrenwend et al. (1992) did find evidence for social drift, even after controlling for socioeconomic class. Also, it is possible that SES level may interact with gender, as males from higher SES homes show poorer clinical outcomes (Parrott & Lewine, 2005). Thus, more work is needed to sort out the relationships between SES and schizophrenia.

PSYCHOLOGICAL AND BIOLOGICAL ASSESSMENT

Diagnostic assessment provides important information about the potential utility of interventions for schizophrenia (e.g., antipsychotic medications). However, assessment does not end with a diagnosis. It must be supplemented with additional psychological and biological assessments.

PSYCHOLOGICAL ASSESSMENT

A wide range of different psychological formulations have been proposed for understanding schizophrenia. For example, there are extensive writings about psychodynamic and psychoanalytic interpretations of schizophrenia. Although this work has made contributions to the further development of these theories, these formulations do not appear to have improved the ability of clinicians to understand persons with

this disorder or led to more effective interventions (Mueser & Berenbaum, 1990). Therefore, the use of projective assessment techniques based on psychodynamic concepts of personality, such as the Rorschach and Thematic Apperception Test, is not considered here.

One of the primary areas to assess is severity of psychotic symptoms, because treatment progression is mainly judged by a reduction of symptoms (Andreasen et al., 2005). This includes an assessment of positive and negative symptoms and general psychopathology due to the high co-morbidity with anxiety and mood disorders. Measures such as the Positive and Negative Syndrome Scale (PANN S; Kay, Fiszbein, & Opler, 1987), the Brief Psychiatric Rating Scale (BPR S; Overall & Gorham, 1962), and the Psychotic Rating Scale (PSYRATS; Haddock, McCarron, Tarrier, & Faragher, 1999) have been frequently used in schizophrenia research and have good psychometric properties. Scales specific to positive (Scale for the Assessment of Positive Symptoms; Andreasen & Olsen, 1982) and negative symptoms (Scale for the Assessment of Negative Symptoms; Andreasen, 1982) can be used for a more in-depth and detailed assessment of these areas. There are also self-report and interview-based measures of insight available as well (see Amador & David, 2004). Commonly, these symptom measures are used in conjunction with a structured diagnostic interview in the assessment of schizophrenia.

As noted earlier, schizophrenia is often associated with a variety of neuropsychological impairments. Core areas to assess in terms of cognitive functioning are verbal and visual learning and memory, working memory, attention/vigilance, abstract reasoning/executive functioning, speed of information processing, and social cognition. These areas are part of the National Institute of Mental Health—Measurement and Treatment Research to Improve Cognition in Schizophrenia cognitive battery (NIMH-MATRICS; Green et al., 2004). Having information on cognitive functioning in these areas will aid in examining the beneficial effects of antipsychotic medication on cognition. It also is important to consider the generalization of these impairments to different situations (i.e., transfer of training problems). Thus, assessment needs to be conducted in the environments in which the skills are to be used in order to provide a more ecologically valid assessment. For example, successful employment interventions incorporate assessment on the job on an ongoing basis rather than extensive prevocational testing batteries that do not generalize to real-world settings (Bond, 1998; Drake & Becker, 1996). Similarly, when assessing independent living skills, it is important that these be measured directly in the living environment of the patient or in simulated tests (Wallace, Liberman, Tauber, & Wallace, 2000).

A great deal of research has been done on the functional assessment of social skills in people with schizophrenia. Social skills refer to the individual behavioral components, such as eye contact, voice loudness, and the specific choice of words, which in combination are necessary for effective communication with others (Mueser & Bellack, 1998). As previously described, poor social competence is a hallmark of schizophrenia. Although not all problems in social functioning are the consequence of poor social skills, many social impairments appear to be related to skill deficits (Bellack, Morrison, Wixted, & Mueser, 1990).

Several different strategies can be used to assess social competence. Clinical interviews can be a good starting place for identifying broad areas of social dysfunction.

These interviews can focus on answering questions such as: Is the patient lonely? Would the patient like more or closer friends? Is the patient able to stand up for his or her rights? Is the patient able to get others to respond positively to him or her? Patient interviews are most informative when combined with interviews with significant others, such as family members and clinicians who are familiar with the nature and quality of the patient's social interactions, as well as naturalistic observations of the patient's social interactions. The combination of these sources of information is useful for identifying specific areas in need of social skills training.

One strategy for assessing social skills that yields the most specific type of information is role-play assessments. Role-plays usually involve brief simulated social interactions between the person and a confederate taking the role of an interactive partner. During role-plays, individuals are instructed to act as though the situation were actually happening in real life. Role-plays can be as brief as 15 to 30 seconds to assess skill areas such as initiating conversations, or they can be as long as several minutes to assess skills such as problem-solving ability. Role-plays can be audiotaped or videotaped and later rated on specific dimensions of social skill. Alternatively, role-playing can be embedded into the procedures of social skills training, in which persons with schizophrenia practice targeted social skills in role-plays, followed by positive and corrective feedback and additional role-play rehearsal. In the latter instance, the assessment of social skills is integrated into the training of new skills, rather than preceding skills training.

A commonly used assessment measure for social skill is the Maryland Assessment of Social Competence (MASC; Bellack & Thomas-Lohrman, 2003). The MASC is a structured role-play assessment that consists of four 3-minute interactions. Following each role-play, ratings on verbal and nonverbal skill and effectiveness are made, thus allowing the clinician to examine social skill across different situations and contexts.

Recent research on the reliability and validity of social skill assessments, and the benefits of social skills training for persons with schizophrenia, has demonstrated the utility of the social skills construct. Persons with schizophrenia have consistently been found to have worse social skills than persons with other psychiatric disorders (Bellack, Morrison, Wixted, et al., 1990; Bellack, Mueser, Wade, Sayers, & Morrison, 1992; Mueser, Bellack, Douglas, & Wade, 1991), and approximately half of the persons with schizophrenia demonstrate stable deficits in basic social skills compared to the nonpsychiatric population (Mueser, Bellack, Douglas, & Morrison, 1991). In the absence of skills training, social skills tend to be stable over periods of time as long as 6 months to 1 year (Mueser, Bellack, Douglas, & Morrison, 1991). Social skill in persons with schizophrenia is moderately correlated with level of premorbid social functioning, current role functioning, and quality of life (Mueser, Bellack, Morrison, & Wixted, 1990). Social skills tend to be associated with negative symptoms (Appelo et al., 1992; Bellack, Morrison, Wixted, et al., 1990; Lysaker, Bell, Zito, & Bioty, 1995; Penn, Mueser, Spaulding, Hope, & Reed, 1995), but not with positive symptoms (Mueser, Douglas, Bellack, & Morrison, 1991; Penn et al., 1995). Furthermore, role-play assessments of social skill are also strongly related with social skill in more natural contexts, such as interactions with significant others (Bellack, Morrison, Mueser, et al., 1990).

Persons with schizophrenia show a wide range of impairments in social skills, including areas such as conversational skill, conflict resolution, assertiveness, and

problem solving (Bellack, Sayers, Mueser, & Bennett, 1994; Douglas & Mueser, 1990). Thus, ample research demonstrates that social skills are impaired with persons with schizophrenia, tend to be stable over time in the absence of intervention, and are strongly related to other measures of social functioning. Furthermore, there is growing evidence supporting the efficacy of social skills training for schizophrenia (Bellack, 2004; Heinssen, Liberman, & Kopelowicz, 2000).

The broadest area of psychological assessment is community functioning, and improvement in this area is linked to the concept of recovery (see "Course and Prognosis"). Persons with schizophrenia show not only poor social skills but also poor adaptive functioning in the community. Ideally, treatment programs should aim to improve the person's quality of life and satisfaction. Independent living skills, quality of life, and social functioning may need to be assessed in order to examine the person's current functional capacity level. The Social Functioning Scale (Birchwood, Smith, Cochrane, Wetton, & Copstake, 1990) and UCSD Performance-Based Skills Assessment (UPSA; Patterson, Goldman, McKibbin, Hughs, & Jeste, 2001) are widely used measures of adaptive and community functioning.

Family Assessment

The assessment of family functioning has high relevance in schizophrenia for two reasons. First, Expressed Emotion (EE), which refers to the presence of hostile, critical, or emotionally overinvolved attitudes and behaviors on the part of close relatives of persons with schizophrenia, is an important stressor that can increase the chance of relapse and rehospitalization (Butzlaff & Hooley, 1998). Second, caring for an individual with a psychiatric illness can lead to a significant burden on relatives (Webb et al., 1998), which ultimately can threaten their ability to continue to provide emotional and material support to the individual. Family burden has its own negative consequences and can be related to EE and the ability of the family to care for the person with schizophrenia. Thus, a thorough assessment of these family factors is important in order to identify targets for family intervention.

Several specific methods can be used to assess a negative emotional climate in the family and the burden of the illness. Interviews with individual family members, including the person with schizophrenia, as well as with the entire family, coupled with observation of more naturalistic family interactions, can provide invaluable information about the quality of family functioning. The vast majority of research on family EE has employed a semistructured interview with individual family members, the Camberwell Family Interview (Leff & Vaughn, 1985). This instrument is primarily a research instrument, and it is too time-consuming to be used in clinical practice. Alternatives to the Camberwell Family Interview have been proposed (e.g., Magaña et al., 1986), although none has gained widespread acceptance yet. Several studies have successfully employed the Family Environment Scale (Moos & Moos, 1981), a self-report instrument completed by family members, which has been found to be related to symptoms and outcome in patients with schizophrenia (Halford, Schweitzer, & Varghese, 1991).

Many instruments have been developed for the assessment of family burden. The most comprehensive instrument, with well-established psychometric properties, is the Family Experiences Interview Schedule (Tessler & Gamache, 1995). This measure

provides information regarding both dimensions of subjective burden (e.g., emotional strain) and objective burden (e.g., economic impact), as well as specific areas in which the burden is most severe (e.g., household tasks). The importance of evaluating family functioning is supported by research demonstrating clinical benefits of family intervention for schizophrenia. Numerous controlled studies of family treatment for schizophrenia have shown that family intervention has a significant impact on reducing relapse rates and rehospitalizations (Dixon et al., 2001; Pitschel-Walz, Leucht, Bäuml, Kissling, & Engel, 2001). The critical elements shared across different models of family intervention are education about schizophrenia, the provision of ongoing support, improved communication skills, and a focus on helping all family members improve the quality of their lives (Dixon & Lehman, 1995; Glynn, 1992; Lam, 1991).

BIOLOGICAL ASSESSMENT

Biological assessments are becoming more common in the clinical management of schizophrenia. For diagnosis, biological assessments may be used to rule out possible organic factors such as a tumor, stroke, or covert substance abuse. Urine and blood specimens are sometimes obtained in order to evaluate the presence of substance abuse. Similarly, blood samples may be obtained in order to determine whether the person is compliant with the prescribed antipsychotic medication, although the specific level of medication in the blood has not been conclusively linked to clinical response. Blood levels may also be monitored to ensure appropriate levels of mood stabilizers (e.g., lithium). Some newer medications (e.g., Clozaril) also require ongoing blood tests to detect very rare, but potentially lethal, blood disorders (Alvir, Lieberman, & Safferman, 1995; Young, Bowers, & Mazure, 1998). Client participation in this type of medical monitoring is crucial when using these medications.

Biological measures are sometimes used to characterize impairments in brain functioning associated with schizophrenia, although these assessments do not have clear implications for treatment of the illness at this time and are expensive. In addition, many clinicians do not have access to imaging technology, and its use has been specific to research settings. In terms of brain function and structure, computerized axial tomography (CAT) scans indicate that between one-half and two-thirds of all persons with schizophrenia display enlarged cerebral ventricles, particularly the lateral and third ventricles, which is indicative of cortical atrophy (Liddle, 1995).

Magnetic resonance imaging (MRI) studies have found structural changes and a reduction in gray matter volumes in the prefrontal, superior temporal, amygdala, hippocampus, and thalamus (Lawrie & Abukmeil, 1998; Wright et al., 2000). These findings have also been found in first-episode and nonill relatives as well and may be a pathophysiological marker for the disorder (Fannon et al., 2000; McDonald et al., 2002). These gross structural impairments in brain functioning, such as enlarged ventricles, tend to be associated with a wide range of neuropsychological impairments and negative symptoms often present in schizophrenia (Andreasen, Flaum, Swayze, Tyrrell, & Arndt, 1990; Buchanan et al., 1993; Merriam, Kay, Opler, Kushner, & van Praag, 1990). In addition, positron emission tomography (PET) and single photon emission computerized tomography (SPECT) have shown reduced metabolism and

blood flow in several of the prefrontal and temporal cortexes, and abnormal activation of the thalamus (Kindermann, Karimi, Symonds, Brown, & Jeste, 1997; Liddle, 1997; McClure, Keshavan, & Pettegrew, 1998; Miyamoto et al., 2003). Functional MRI (fMRI) studies have found less activation in the prefrontal cortex and anterior cingulate cortex during working memory tasks (Carter, MacDonald, Ross, & Stenger, 2001; Perlstein, Carter, Noll, & Cohen, 2001). Finally, diffuse tensor imaging methods, which assess the integrity of white matter pathways in the brain, have found problems in myelinated neurons in the prefrontal lobes specifically and in the connections between the frontal, temporal, and parietal lobes (Burns et al., 2003; Lim, Hedehus, deCrespigny, Menon, & Moseley, 1998).

To date, most of the advances in the treatment of schizophrenia have been in psychopharmacology. Biological assessments are still not useful for diagnosing the illness or for guiding treatment. However, the clinical utility of biological assessment is likely to increase in the years to come as advances continue to be made in the understanding of the biological roots of schizophrenia.

ETIOLOGICAL CONSIDERATIONS

Behavioral Genetics and Molecular Genetics

The etiology of schizophrenia has been a topic of much debate over the past 100 years. Kraepelin (1919/1971) and Bleuler (1911/1950) clearly viewed the illness as having a biological origin. However, from the 1920s to the 1960s, alternative theories gained prominence, speculating that the disease was the result of disturbed family interactions (Bateson, Jackson, Haley, & Weakland, 1956). Psychogenic theories of the etiology of schizophrenia, positing that the illness was psychological in nature rather than biological, played a dominant role in shaping the attitudes and behavior of professionals toward persons with schizophrenia and their relatives (Fromm-Reichmann, 1950; Searles, 1965). These theories have not been supported empirically (Jacob, 1975; Waxler & Mishler, 1971). Moreover, in many cases, psychogenic theories fostered poor relationships between mental health professionals and relatives (Terkelsen, 1983), which have only begun to mend in recent years (Mueser & Glynn, 1999). For more than a century, clinicians have often noted that schizophrenia tends to "run in families." However, the clustering of schizophrenia in family members could reflect learned behavior that is passed on from one generation to the next, rather than predisposing biological factors.

In the 1950s and 1960s, two paradigms were developed for evaluating the genetic contributions to the illness. The first approach, the high-risk paradigm, involves examining the rate of schizophrenia in adopted-away or biological offspring of mothers with schizophrenia. If the rate of schizophrenia in children of biological parents with schizophrenia is higher than in the general population, then even in the absence of contact with those parents, a role for genetic factors in developing the illness is supported. The second approach, the monozygotic/dizygotic twin paradigm, involves comparing the concordance rate of schizophrenia in identical twins (monozygotic) compared to fraternal twins (dizygotic). Because monozygotic twins share the exact same gene pool, whereas dizygotic twins share only approximately half their genes, a higher concordance rate of schizophrenia among monozygotic

twins than dizygotic twins, even reared in the same environment, would support a role for genetic factors in the etiology of schizophrenia.

Over the past 30 years, numerous studies employing either the high-risk or twin paradigm have been conducted examining the role of genetic factors in schizophrenia. There has been almost uniform agreement across studies indicating that the risk of developing schizophrenia in biological relatives of persons with schizophrenia is greater than in the general population, even in the absence of any contact between the relatives (Kendler & Diehl, 1993). Thus, support exists for the role of genetic factors in the etiology of at least some cases of schizophrenia. For example, the odds of developing schizophrenia if one parent has the disorder is 13% and rises to about 50% if both parents have the disorder, compared to only 1% risk in the general population (Gottesman, 1991, 2001; McGuffin, Owen, & Farmer, 1995). Similarly, the concordance rate of one identical twin developing schizophrenia if his or her co-twin also has schizophrenia is between 25% and 50%, compared to about 6% and 15% for fraternal twins (Cardno et al., 1999; Faraone & Tsuang, 1985; Torrey, 1992; Walker, Downey, & Caspi, 1991). It also appears that the risk of developing schizophrenia is greater in more severe types of schizophrenia (average 20% for disorgranized and catatonic types; see Gottesman & Shields, 1982).

The fact that identical twins do not have a 100% concordance rate of schizophrenia (heritability rates = 0.80 on average), as might be expected if the disorder were purely genetic, has raised intriguing questions about the etiology of schizophrenia. In a review of 40 studies on genetic risk, it was found that 80% of persons with psychotic symptoms do not have a single parent with the disorder, and 60% have a negative family history (Gottesman, 2001). It is likely that the development of schizophrenia results from an interaction between genetic and environmental factors. The results of a series of longitudinal studies support this case. Tienari (1991; Tienari et al., 1987; Tienari et al., 2004) compared the likelihood of developing schizophrenia in three groups of children raised by adoptive families. Two groups of children had biological mothers with schizophrenia, and the third group had biological mothers with no psychiatric disorder. The researchers divided the adoptive families of the children into two broad groups based on the level of disturbance present in the family: healthy adoptive families and disturbed adoptive families. Follow-up assessments were conducted to determine the presence of schizophrenia and other severe psychiatric disorders in the adopted children raised in all three groups. The researchers found that biological children of mothers with schizophrenia who were raised by adoptive families with high levels of disturbance were significantly more likely to develop schizophrenia or another psychotic disorder (46%) than either similarly vulnerable children raised in families with low levels of disturbance (5%) or children with no biological vulnerability raised in either disturbed (24%) or healthy (3%) adoptive families. This study raises the intriguing possibility that some cases of schizophrenia develop as a result of the interaction between biological vulnerability and environmental stress.

Although families do not cause schizophrenia, there are important interactions between the family and person with schizophrenia that deserve consideration. First, as previously mentioned, it has repeatedly been found that critical attitudes and high levels of emotional overinvolvement (Expressed Emotion [EE]) on the part of the relatives toward the individual with schizophrenia are strong predictors of

the likelihood that persons with schizophrenia will relapse and be rehospitalized (Butzlaff & Hooley, 1998). The importance of family factors is underscored by the fact that the severity of persons' psychiatric illness or their social skill impairments is not related to family EE (Mueser et al., 1993). Rather, family EE seems to act as a stressor, increasing the vulnerability of persons with schizophrenia to relapse.

A second important family consideration is the amount of burden on relatives caring for a mentally ill person. Family members of persons with schizophrenia typically experience a wide range of negative emotions related to coping with the illness, such as anxiety, depression, guilt, and anger (Hatfield & Lefley, 1987, 1993; Oldridge & Hughes, 1992). Burden is even associated with negative health consequences for relatives (Dyck, Short, & Vitaliano, 1999). Family burden may be related to levels of EE, ability to cope with the illness, and ultimately the ability of the family to successfully monitor and manage the schizophrenia in a family member (Mueser & Glynn, 1999). Thus, EE and family burden are important areas for assessment and intervention. Finally, researchers have been interested in discovering genes and chromosomal areas involved in schizophrenia.

Current research has focused on nine chromosomes (i.e., most important appear to be areas 8p and 22q) and seven candidate genes, which may be important in schizophrenia (see Harrison & Owen, 2003). In particular, researchers are particularly interested in identifying genes found across family members with the disorder (linkage studies) or directly related to the underlying pathophysiology of schizophrenia (e.g., genes that affect neurotransmitter functioning such as dopamine, serotonin, or glutamate). This area of research has been hampered by the lack of independent replication of these genetic markers. The exact mechanism for genetic transmission of the disorder is unknown, but it appears that schizophrenia does not follow a Mendelian single gene pattern of inheritance. It is more likely that schizophrenia is a polygenetic condition or that it arises from an interaction of multiple genes, which increase the susceptibility to the disorder (Craddock, O'Donovan, & Owen, 2006; Miyamoto et al., 2003). Regardless, genes and gene-environment interactions are estimated to account for 80% of the risk for schizophrenia, according to a review of the literature (as reviewed in Tandon et al., 2008b).

Neuroanatomy and Neurobiology

Although there is clear evidence that genetic factors can play a role in the development of schizophrenia, there is also a growing body of evidence pointing to the influence of other biological, nongenetic factors playing a critical role. For example, obstetric complications, maternal exposure to the influenza virus, and other environmental-based insults to the developing fetus (e.g., maternal starvation) are all associated with an increased risk of developing schizophrenia (Geddes & Lawrie, 1995; Kirch, 1993; Rodrigo, Lusiardo, Briggs, & Ulmer, 1991; Susser & Lin, 1992; Susser et al., 1996; Takei et al., 1996; Thomas et al., 2001; Torrey, Bowler, Rawlings, & Terrazas, 1993). Thus, there is a growing consensus that the etiology of schizophrenia may be heterogeneous, with genetic factors playing a role in the development of some cases and early environmental-based factors playing a role in the development of other cases. This heterogeneity may account for the fact that the genetic contribution to schizophrenia has consistently been found to be lower than the genetic contribution to bipolar

disorder (Goodwin & Jamison, 1990). Other biological and physiological factors include alterations in brain chemistry and structure.

Pharmacological research has identified many neurochemical changes associated with schizophrenia. By far, the neurotransmitter most commonly implicated in the onset of schizophrenia is dopamine. The dopamine hypothesis proposes that alterations in levels of dopamine are responsible for the symptoms of schizophrenia. Originally, this hypothesis was based on findings that substances that increase dopamine (e.g., levadopa used to treat Parkinson's disease) increase psychotic symptoms, and substances that decrease dopamine reduce psychotic symptoms. Current versions of this hypothesis suggest that an overabundance of dopamine in certain limbic areas of the brain may be responsible for positive symptoms, whereas a lack of dopamine in cortical areas may be responsible for negative symptoms (Davis, Kahn, Ko, & Davidson, 1991; Moore, West, & Grace, 1999). Other neurochemicals also appear to be implicated in schizophrenia. In particular, serotonin may directly or indirectly (e.g., by mediating dopamine) affect symptoms of schizophrenia, because several of the newer antipsychotic medications impact serotonin levels (Lieberman et al., 1998). In addition, glutamate and GABA may be altered in schizophrenia (Pearlson, 2000).

As discussed in the section "Biological Assessment," abnormalities in several brain structures have also been identified. In particular, enlarged ventricles and decreased brain volume and blood flow to cortical areas have been associated with a wide range of cognitive impairments and negative symptoms of schizophrenia (Andreasen et al., 1990; Buchanan et al., 1993; Merriam et al., 1990).

LEARNING, MODELING, AND LIFE EVENTS

Although schizophrenia is broadly accepted to be a biologically based disorder and not a learned one, learning and modeling may play a role in the course, outcome, and symptom expression of the disorder. In terms of symptom expression, there is empirical support for the role of operant conditioning in delusions and hallucinations (e.g., hallucinations increase when reinforced). Furthermore, research has shown that psychotic behavior can be modified using differential reinforcement (i.e., attention for any other behavior besides the expression of delusional statements) or punishment principles (Jimenez, Todman, Perez, Godoy, & Landon-Jimenez, 1996; Schock, Clay, & Cipani, 1998). However, these processes are probably more relevant for the maintenance of psychotic symptoms than for etiology. Haynes (1986) proposed a behavioral model of paranoia in which suspiciousness partially stems from the reinforcement of paranoid statements and parental modeling, but this theory has been largely untested.

As described in the following section, the stress-vulnerability model of schizophrenia posits that coping skills mediate the noxious effects of stress on psychobiological vulnerability to symptoms and relapses (Liberman et al., 1986; Nuechterlein & Dawson, 1984). Coping skills, such as social skills for developing and maintaining close relationships with others and strategies for managing negative emotions and distorted thinking processes, can be acquired either naturalistically through access to good role models (e.g., family, friends) or through social learning-based programs, such as social skills training (Bellack, Mueser, Gingerich, & Agresta, 1997) or cognitive-behavior therapy (Chadwick & Birchwood, 1995; Fowler, Garety, & Kuipers, 1995).

Thus, improving coping skills, as well as other life skills, through the systematic application of social learning methods is a common treatment goal in schizophrenia.

Although stressful life events alone are not the cause of schizophrenia, some theories hypothesize that life events may contribute to the development of the disorder and can play an important role in the course of schizophrenia. The stress-vulnerability model (Liberman et al., 1986; Zubin & Spring, 1977) assumes that symptom severity and related impairments of psychiatric disorders such as schizophrenia have a biological basis (psychobiological vulnerability) determined by a combination of genetic and early environmental factors. This vulnerability can be decreased by medications and worsened by substance use disorder. Stress, including discrete events such as traumas and exposure to ongoing conditions such as a hostile environment, can impinge on vulnerability, precipitating relapses and worse outcomes. Finally, coping resources, such as coping skills or the ability to obtain social support, can minimize the effects of stress on relapse and the need for acute care.

As described earlier, EE represents a stressful familial environment that may increase relapse and hospitalization in people with schizophrenia. In addition, in the "Clinical Picture" section, we discussed that people with schizophrenia are often the targets of violence and have frequently been exposed to physical and/or sexual assault. Exposure to traumatic events may lead to PTSD, a condition characterized by reliving the traumatic experience (e.g., nightmares, intrusive memories), avoidance of people, places, and things that remind the person of the event, and increased arousal symptoms (e.g., irritability, sleep problems). Exposure to trauma and the presence of PTSD are likely to worsen the course of schizophrenia and complicate treatment (Mueser, Rosenberg, Goodman, & Trumbetta, 2002). For example, research shows that both discrete stressors (e.g., life events) and exposure to a stressful environment can worsen psychotic disorders (Butzlaff & Hooley, 1998). PTSD is also associated with substance abuse (Chilcoat & Breslau, 1998), which, as described earlier, can have severe consequences for people with schizophrenia.

Cognitive Influences

Cognitive impairments refer to difficulties in verbal and visual learning and memory, working memory, attention/vigilance, abstract reasoning/executive functioning (i.e., understanding a concept, planning, organizing), and speed of information processing (Green et al., 2004). These cognitive deficits have been observed in unmedicated, medicated, first-episode, remitted, and high-risk children prior to developing the disorder. Thus, cognitive impairments are so commonplace that they are now considered a core feature of schizophrenia (Palmer et al., 1997; Wilk et al., 2005). A recent meta-analysis of cognitive performance found that normal controls without a history of schizophrenia perform consistently better (about 1 standard deviation) than persons with schizophrenia on most cognitive tasks, which suggests that a generalized cognitive deficit is present (Heinrichs, 2005). These deficits also appear to be relatively stable over time and do not appear to reflect a progressive deterioration (Heaton et al., 2001). These cognitive impairments may interfere with the person's ability to focus for sustained periods on work or recreational pursuits, interact effectively with others, perform basic activities of daily living, or participate in conventional psychotherapeutic interventions (Bellack, Gold, & Buchanan, 1999; Brekke, Raine, Ansel,

Lencz, & Bird, 1997; Green, Kern, Braff, & Mintz, 2000; Sevy & Davidson, 1995; Velligan et al., 1997). Cognitive impairments also result in difficulties with generalizing training or knowledge to other areas (i.e., transfer of training problems) (Mueser, Bellack, Douglas, & Morrison, 1991; Smith, Hull, Romanelli, Fertuck, & Weiss, 1999). Thus, many rehabilitative efforts focus on teaching persons with schizophrenia directly in the environment in which skills will be used or involve specialized teaching methods, such as errorless learning procedures (Kern, Liberman, Kopelowicz, Mintz, & Green, 2002).

In addition to cognitive deficits, it has become apparent that impairments in social cognition (defined as the way people perceive, interpret, and understand social information) are also found in schizophrenia (Penn, Corrigan, Bentall, Racenstein, & Newman, 1997). Deficits in emotion and social cue perception, problems inferring the intentions and motivations of others (Theory of Mind), and impairments in social knowledge and schemata have all been found in schizophrenia (Brune, 2005; Corrigan & Penn, 2001; Edwards, Jackson, & Pattison, 2002). More specifically, persons with persecutory delusions exhibit an attributional style in which they tend to blame others rather than situations for negative events (e.g., personalizing attributional style; see Garety & Freeman, 1999). Deficits in social cognition appear to be independent from nonsocial cognition (e.g., memory, attention) in that they predict incremental variance in social functioning and social skill and may arise from distinct brain structures involved in social information processing (Penn, Combs, & Mohamed, 2001; Penn et al., 1997; Pinkham, Penn, Perkins, & Lieberman, 2003). The exact nature of the relationship between social cognition and cognitive functioning is unclear, but social cognition appears to be important in the social functioning of persons with schizophrenia (Green, Oliver, Crawley, Penn, & Silverstein, 2005).

SEX AND RACIAL-ETHNIC CONSIDERATIONS

Several issues related to gender are important for understanding the psychopathology in the course of schizophrenia. As described in the section on course and prognosis, women tend to have a milder overall course and later onset of schizophrenia than do men. The net consequence of this is that, although similar numbers of men and women have schizophrenia, men are more likely to receive treatment for the disorder. In fact, most research on the treatment of schizophrenia is conducted on samples ranging from 60% to 100% male.

Because treatment studies usually sample persons with schizophrenia who are currently receiving treatment, often inpatient treatment, the efficacy of widely studied psychosocial interventions, such as social skills training and family therapy, has been less adequately demonstrated in women. For example, some research suggests that social skills training may be more helpful to men than to women (Mueser, Levine, Bellack, Douglas, & Brady, 1990; Schaub, Behrendt, Brenner, Mueser, & Liberman, 1998; Smith et al., 1997). There is a need for more research on the effects of treatments for women with schizophrenia. At the same time, further consideration needs to be given to the different needs of women with this illness. For example, women with schizophrenia are much more likely than men to marry and have children. It is crucial, therefore, that psychosocial interventions be developed to address the relationship,

family planning, and parenting needs of women with schizophrenia (Apfel & Handel, 1993; Brunette & Dean, 2002; Coverdale & Grunebaum, 1998).

Another issue related to gender in need of further consideration is exposure to trauma. As described earlier, people with schizophrenia are at risk for being the victims of violence. Although both men and women with schizophrenia report histories of abuse and assault, women report more sexual assault (Goodman et al., 2001; Mueser et al., 1998). Furthermore, in the general population, women are more likely to be abused than men, are more likely to sustain injuries, and are more likely to be economically dependent upon perpetrators of domestic violence. Thus, there is a particular need to recognize and address trauma in the lives of women with schizophrenia. Accurate detection of trauma is further complicated by the fact that most severely mentally ill persons who have been physically or sexually assaulted deny that they have been abused (Cascardi et al., 1996). The development of programs that address both the causes of domestic violence and their sequelae, especially for women with schizophrenia, is a priority in this area (Harris, 1996; Rosenberg et al., 2001).

Research on the relationships between race, ethnicity, and severe psychiatric disorders demonstrates that cultural factors are critical to understanding how persons with schizophrenia are perceived by others in their social milieu, as well as the course of the illness. Although the prevalence of schizophrenia is comparable across different cultures, several studies have shown that the course of the illness is more benign in developing countries compared to industrialized nations (Lo & Lo, 1977; Murphy & Raman, 1971; Sartorius et al., 1986). Westermeyer (1989) has raised questions about the comparability of clinical samples in cross-cultural studies, but a consensus remains that the course of schizophrenia tends to be milder in nonindustrialized countries (Jablensky, 1989).

A variety of different interpretations have been offered to account for the better prognosis of schizophrenia in some cultures (Lefley, 1990). It is possible that the strong stigma and social rejection that results from serious mental illness and poses an obstacle to the ability of persons with schizophrenia to cope effectively with their disorder and assimilate into society (Fink & Tasman, 1992) is less prominent in some cultures (Parra, 1985). Greater cultural, familial, and societal acceptance of the social deviations present in schizophrenia may enable these persons to live less stressful and more productive lives. This may be especially true for Hispanic families, who show less expressed emotion as compared to White families (Dorian, Garcia, Lopez, & Hernandez, 2008; Lopez et al., 2009). Hispanic families are typically characterized as more accepting and less blaming of persons with schizophrenia (Kymalainen & Weisman de Mamani, 2008). This is important given the link between EE and relapse and, in fact, lower rates of relapse have been found in minority families (Aguilera, Lopez, Breitborde, Kopelowicz, & Zarate, 2010).

Cultures with a stronger degree of family ties, in particular, may be less vulnerable to the effects of mental illness (Lin & Kleinman, 1988). For example, Liberman (1994) has described how the strong functional ties of seriously mentally ill persons to their families and work foster the reintegration of persons with schizophrenia back into Chinese society following psychiatric hospitalization. In contrast, until recently, families of persons with schizophrenia in many Western societies were viewed by mental health professionals as either irrelevant, or worse, as causal agents in the

development of the illness (Lefley, 1990; Mueser & Glynn, 1999), thus precluding them from a role in psychiatric rehabilitation. Furthermore, the use of other social supports may vary across different ethnic groups or cultures, such as the importance of the church to the African American community and its potential therapeutic benefits (Griffith, Young, & Smith, 1984; Lincoln & Mamiya, 1990).

Some have hypothesized that different cultural interpretations of the individual's role in society and of the causes of mental illness may interact to determine course and outcome. Estroff (1989) has suggested that the emphasis on the self in Western countries, compared to a more family or societally based identification, has an especially disabling effect on persons with schizophrenia, whose sense of self is often fragile or fragmented. Another important consideration is the availability of adaptive concepts for understanding mental illness. For example, *espiritismo* in Puerto Rican culture is a system of beliefs involving the interactions between the invisible spirit world and the visible world, in which spirits can attach themselves to persons (Comas-Díaz, 1981; Morales-Dorta, 1976). Spirits are hierarchically ordered in terms of their moral perfection, and the practice of *espiritismo* is guided by helping individuals who are spiritually ill to achieve higher levels of this perfection. Troubled persons are not identified as sick, nor are they blamed for their difficulties; in some cases, symptoms such as hallucinations may be interpreted favorably as signs that the person is advanced in his or her spiritual development, resulting in some prestige (Comas-Díaz, 1981). Thus, certain cultural interpretations of schizophrenia may promote more acceptance of persons who display the symptoms of schizophrenia, as well as avoiding the common assumption that these phenomenological experiences are the consequence of a chronic, unremitting condition.

Understanding different cultural beliefs, values, and social structures can have important implications for the diagnosis of schizophrenia. Religious practices and beliefs may complicate diagnosis. For example, high levels of religiosity have been found in people with schizophrenia (Brewerton, 1994). Without a clear understanding of the religious and cultural background, patients may be misdiagnosed (May, 1997). Ethnic groups may differ in their willingness to report symptoms, as illustrated by one study that reported that African American persons were less likely than Hispanics or non-Hispanic Whites to report symptoms (Skilbeck, Acosta, Yamamoto, & Evans, 1984). Several studies have shown that ethnic differences in diagnosis vary as a function of both the client's and the interviewer's ethnicity (Baskin, Bluestone, & Nelson, 1981; Loring & Powell, 1988). Misdiagnosis of mood disorders as schizophrenia is the most common problem with the diagnosis of ethnic minorities in the United States (e.g., Jones, Gray, & Parsons, 1981, 1983).

Other studies have found that African Americans are more likely than Whites to be inappropriately diagnosed with paranoid schizophrenia, which has been viewed as a clinician bias in the interpretation of mistrust (Adams, Dworkin, & Rosenberg, 1984; Combs, Penn, & Fenigstein, 2002; Combs et al., 2006; Whaley, 1997, 2001). Alternatively, this finding may also represent the effects of stress and poverty in the development of schizophrenia given the numbers of minorities who live in poverty (Bruce, Takeuchi, & Leaf, 1991; as discussed in "Epidemiology"). Knowledge of cultural norms appears critical to avoid the possible misinterpretation of culturally bound beliefs, experiences, and practices when arriving at a diagnosis.

Cultural differences are also critical in the treatment of schizophrenia, both with respect to service utilization and the nature of treatment provided. There is a growing body of information documenting that ethnic groups differ in their use of psychiatric services. Several studies have indicated that Hispanics and Asian Americans use fewer psychiatric services than non-Hispanic Whites, whereas Blacks use more emergency and inpatient services (Cheung & Snowden, 1990; Hough et al., 1987; Hu, Snowden, Jerrell, & Nguyen, 1991; Padgett, Patrick, Burns, & Schlesinger, 1994; Sue, Fujino, Hu, Takeuchi, & Zane, 1991). Aside from cultural-based practices that may cause some individuals to seek assistance outside the mental health system (e.g., practitioners of santería; González-Wippler, 1992), access to and retention in mental health services may be influenced by the proximity of mental health services (Dworkin & Adams, 1987) and by the ethnicity of treatment providers. Sue et al. (1991) reported that matching clinician and client ethnicity resulted in higher retention of ethnic minorities in mental health services. Increasing access to needed services for racial/ethnic minorities may require a range of strategies, including ensuring that services are available in the communities where clients live, working with the natural social supports in the community, awareness of relevant cultural norms, and adequate representation of ethnic minorities as treatment providers.

Cultural factors may have an important bearing on psychotherapeutic treatments provided for schizophrenia. Sue and Sue (1990) have described the importance of providing psychotherapy driven by goals that are compatible with clients' cultural norms. This requires both knowledge of subcultural norms and familiarity with the other social support mechanisms typically available to those individuals. Interventions developed for one cultural group may need substantial modification to be effective in other groups. For example, Telles et al. (1995) reported that behavioral family therapy, which has been found to be effective at reducing relapse in schizophrenia for samples of non-Hispanic White and African American individuals (Mueser & Glynn, 1999), was significantly less effective for Hispanic Americans (of Mexican, Guatemalan, and Salvadoran descent) with low levels of acculturation than for more acculturated individuals. In addition, behavioral family therapy has been found to be effective when implemented in Spain and China (Montero et al., 2001; Xiong et al., 1994; Zhang, Wang, Li, & Phillips, 1994). These findings underscore the importance of tailoring psychosocial interventions to meet the unique needs of clients from different cultural backgrounds.

A final cultural factor is stigma—that is, negative attitudes that lead to prejudice and discrimination against people with schizophrenia. Although stigma can be present for a variety of disabilities, attitudes toward people with serious mental illness tend to be more negative (Corrigan & Penn, 1999). Stigma may stem from characteristics of the disorder itself, such as poor social skills, bizarre behavior, and unkempt appearance, and stigma may develop and be maintained through negative media portrayals and myths (e.g., dangerousness, unpredictability) (Farina, 1998). Stigma and discrimination can greatly undermine the person's ability to recover from the effects of schizophrenia and integrate into society. For example, people with serious mental illness identify role functioning, such as employment, developing and maintaining friendships and intimate relationships, and regular activities as critical to their recovery (Uttaro & Mechanic, 1994). However, many studies have shown that these are the very areas most affected by stigma (Farina, 1998). Much is being done to

try to reduce stigma associated with schizophrenia and other mental illness. In particular, strategies that involve active education and increased contact with people with mental illness (best if same status and background) may be most effective for eradicating this serious problem (Corrigan & Penn, 1999).

COURSE AND PROGNOSIS

Schizophrenia usually has an onset in late adolescence or early adulthood, most often between the ages of 16 and 25. However, there is evidence that signs of the disorder are present long before the clinical symptoms of psychosis appear. Children who later develop schizophrenia show impairments in sociability, emotional expressiveness (less positive and more negative facial expressions), and neuromotor functioning (Schiffman et al., 2004; Walker, Grimes, Davis, & Smith, 1993). Data from the New York High Risk Project, which followed a cohort of children at high risk for schizophrenia, found that deficits in verbal memory, attentional vigilance, and gross motor skills in childhood (ages 7 to 12) predicted the development of schizophrenia later in life (Erlenmeyer-Kimling et al., 2000).

Some individuals display a maladaptive pattern of behaviors, including disruptive behavior, problems in school, poor interpersonal relationships, and impulsivity (Amminger et al., 1999; Baum & Walker, 1995; Fuller et al., 2002; Hans, Marcus, Henson, Auerbach, & Mirsky, 1992). Similarly, symptoms of conduct disorder in childhood, such as repeated fighting, truancy, and lying, have been found to be predictive of the later development of schizophrenia (Asarnow, 1988; Cannon et al., 1993; Neumann, Grimes, Walker, & Baum, 1995; Robins, 1966; Robins & Price, 1991; Rutter, 1984; Watt, 1978). However, other persons with schizophrenia display no unusual characteristics in their premorbid functioning or competence (Zigler & Glick, 1986). The signs of schizophrenia in childhood may be subtle, irregular, and gradual in onset, but they become increasingly more apparent as adolescence approaches (Dworkin et al., 1991).

Prior to the emergence of schizophrenia, many persons enter a prodromal period of the illness, which is characterized by changes in mood and behavior (Yung & McGorry, 1996). The prodrome is an intensification of the core features of the disorder that can last up to 5 years. Prodromal symptoms are subclinical or attenuated symptoms that fail to reach the threshold for a clinical diagnosis but become increasingly apparent to others. Disruptions in sleep, anxiety, depression, aggression/irritability, paranoia, and odd beliefs are common in the prodromal phase (Häfner, Maurer, Trendler, an der Heiden, & Schmidt, 2005; Malla & Payne, 2005; Norman, Scholten, Malla, & Ballageer, 2005; Yung & McGorry, 1996). Social isolation, withdrawal, changes in role functioning, and avolition may be present during this stage as well.

The initial emergence of clinical symptoms (first-episode or first break) is a crucial time for treatment and intervention (Lincoln & McGorry, 1995). It is widely believed that the earlier antipsychotic medications are initiated, the better the long-term outcome becomes (Penn, Waldheter, Perkins, Mueser, & Lieberman, 2005). In fact, a critical time for treatment appears to be during the first 5 years of the disorder (Malla, Norman, & Joober, 2005). This finding, combined with the efficacy of antipsychotic medications (50% show remission after 3 months and 80% show remission at 1 year; as

reviewed in Penn et al., 2005) in first-episode individuals, makes early intervention programs a crucial aspect of treatment. Unfortunately, even after symptom remission is attained, most individuals with schizophrenia still have deficits in social, vocational, and community functioning (Tohen et al., 2000). Negative symptoms in first-episode individuals have been linked to poor cognitive functioning and longer durations of untreated psychosis (Malla & Payne, 2005).

It is extremely rare for the first onset of schizophrenia to occur before adolescence (e.g., before the age of 12), with most diagnostic systems considering childhood-onset schizophrenia to be a different disorder than adolescent or adult onset. More common than childhood schizophrenia, but nevertheless rare in the total population of persons with schizophrenia, are individuals who develop the illness later in life, such as after the age of 40 (late-onset schizophrenia) or after the age of 60 (very-late-onset schizophrenia) (Cohen, 1990; Howard, Rabins, Seeman, Jeste, & the International Late-Onset Schizophrenia Group, 2000). It is estimated that approximately 23% of individuals with schizophrenia develop symptoms after the age of 40 (Harris & Jeste, 1988). Late-onset schizophrenia is more common in women, and there is evidence of better social, educational, and occupational functioning as compared to early-onset schizophrenia (Howard et al., 2000).

Late-onset schizophrenia is more likely to involve positive symptoms (visual, tactile, and olfactory hallucinations; persecutory delusions) and less likely to involve formal thought disorder or negative symptoms (Bartels, Mueser, & Miles, 1998). Late-onset schizophrenia is further complicated by the lack of clear-cut distinguishing characteristics that discriminate this disorder from a variety of other disorders that develop later in old age such as dementia (Howard, Almeida, & Levy, 1994). Thus, it is important to emphasize that the symptoms of schizophrenia can arise at any point in life and are a developmental phenomenon.

The onset, course, and prognosis of the illness are closely tied to gender (Haas & Garratt, 1998). Women tend to have later age of onset of the illness (average onset is between 25 to 29 years), spend less time in hospitals, have fewer negative symptoms, demonstrate less cognitive impairment, and have better social competence and social functioning than men with the illness (Goldstein, 1988; Häfner et al., 1993; Leung & Chue, 2000; Mueser, Bellack, Morrison, & Wade, 1990; Salem & Kring, 1998). The benefits experienced by women do not appear to be explained by societal differences in tolerance for deviant behavior. A variety of different hypotheses have been advanced to account for the superior outcome of women with schizophrenia (e.g., role of estrogen on dopamine receptors, more adaptive coping with socio-environmental stressors, improved social networks and competence [Castle & Murray, 1991; Flor-Henry, 1985; Halari et al., 2004]), but no single theory has received strong support.

In general, the onset of schizophrenia can be described as either gradual or acute. The gradual onset of schizophrenia can take place over many months or years, and it may be difficult for family members and others to clearly distinguish onset of the illness (prepsychotic and prodromal signs). In other cases, the symptoms develop rapidly over a period of a few weeks with dramatic and easily observed changes occurring over this time. People with acute onset of schizophrenia have a somewhat better prognosis than those with a more insidious illness (Fenton & McGlashan, 1991; Kay & Lindenmayer, 1987).

Although schizophrenia is a long-term and severe psychiatric illness, there is considerable interindividual variability in the course and outcome of the illness over time (Marengo, 1994). Generally, though, once schizophrenia has developed, the illness usually continues to be present at varying degrees of severity throughout most of the person's life. Schizophrenia is usually an episodic illness with periods of acute symptom exacerbation (i.e., relapse) requiring more intensive, often inpatient, treatment interspersed by periods of higher functioning between episodes (i.e., remission). Preventing relapse is a significant clinical concern, because each relapse leads to more persistent symptoms and greater cognitive and psychosocial impairment. Although most persons with schizophrenia live in the community, it is comparatively rare, at least in the short term, for individuals to return to their premorbid levels of functioning between episodes.

Remission is the reduction of active symptoms to nonproblematic, less severe levels (Andreasen et al., 2005). Recovery is much broader and includes both symptom remission and an improvement in social, community, occupational, and adaptive functioning. Recovery is also largely based on consumer perceptions of improvement. A recent review of 10 longitudinal studies on outcome in schizophrenia, some of which followed individuals for more than 20 years, reported that between 21% and 57% of persons with schizophrenia showed periodic episodes of recovery (improved symptoms; greater social, educational, and occupational functioning; Jobe & Harrow, 2005). In fact, some of these individuals showed extended periods of recovery without mental health treatment (Harrow, Grossman, Jobe, & Herbener, 2005; Jobe & Harrow, 2005).

Some general predictors of the course and outcome of schizophrenia have been identified, such as premorbid functioning, but overall, the ability to predict outcome is rather poor (Avison & Speechley, 1987; Tsuang, 1986). The primary reason for this is that symptom severity and functioning are determined by the dynamic interplay between biological vulnerability, environmental factors, and coping skills (Nuechterlein & Dawson, 1984; Liberman et al., 1986). Factors such as compliance with medication (Buchanan, 1992), substance abuse (Drake, Osher, & Wallach, 1989), exposure to a hostile or critical environment (Butzlaff & Hooley, 1998), the availability of psychosocial programming (Bellack & Mueser, 1993), and assertive case management and outreach (Mueser, Bond, Drake, & Resnick, 1998; Mueser, Drake, & Bond, 1997; Phillips et al., 2001; Quinlivan et al., 1995) are all environmental factors that in combination play a large role in determining outcome.

The importance of environmental factors and rehabilitation programs in determining the outcome of schizophrenia is illustrated by two long-term outcome studies conducted by Harding and associates (DeSisto, Harding, McCormick, Ashikaga, & Brooks, 1995; Harding, Brooks, Ashikaga, Strauss, & Breier, 1987a, 1987b). The first study was conducted in Vermont, which had a highly developed system of community-based rehabilitation programs for persons with severe mental illness. Persons with schizophrenia in this study demonstrated surprisingly positive outcomes (60% recovery rate) over the 20- to 40-year follow-up period. In contrast, similar individuals in Maine, where more traditional hospital-based treatment programs existed, fared substantially worse over the long-term course of their illness. Thus, the outcome of most cases of schizophrenia is not predetermined by specific biological factors, but rather is influenced by the interaction between biological and environmental factors.

In summary, the prognosis of schizophrenia is usually considered poor to fair, and there is general agreement that it is worse than that for other major psychiatric disorders, such as bipolar disorder or major depression (Jobe & Harrow, 2005). Despite the widespread acceptance that schizophrenia is usually a lifelong disability, recent research on the long-term outcome of schizophrenia has challenged this assumption. Many persons with schizophrenia can attain symptom remission and recovery with the appropriate pharmacological and psychosocial treatment (Ciompi, 1980; Harding et al., 1987a, 1987b; Harrow et al., 2005).

CASE STUDY

Case Identification

Isaac is a 30-year-old, never-married man who lives independently and receives Social Security Supplemental Income because of impaired functioning due to schizophrenia, which developed approximately 10 years ago. Isaac maintains close contact with his parents, who live in the same town, and has occasional contact with his two older brothers and a younger sister. Isaac receives outpatient treatment at his local community mental health center, including antipsychotic medications, involvement in a group program aimed at teaching him how to manage his illness, and participation in a supported employment program that helps him maintain a part-time competitive job at a local grocery store.

Presenting Complaints

Isaac is dissatisfied with several areas of his life that are the focus of treatment. Although medication significantly reduced many of his paranoid symptoms, he continues to have suspicious thoughts in some social situations and feels anxious around other people. He has few friends, none of them women, and he would like to have more friends, including a girlfriend. Although his hygiene is generally good, when his psychotic symptoms increase, he becomes more disheveled, smokes more cigarettes, and becomes agitated. In addition to Isaac's mild paranoia and social anxiety, his social skills are not strong. For example, Isaac maintains poor eye contact and speaks in a low tone of voice when talking with other people, he rarely smiles spontaneously, and he has difficulty coming up with interesting conversational topics. Isaac is also dissatisfied with not completing his college degree because his three siblings have all graduated college, but he doesn't want to return to school until he has proved to himself that he can hold down his part-time job. He has a very low energy level and sometimes has trouble following through regularly on his goals, including his part-time job. Isaac recognizes that he has problems and needs help, but he lacks basic insight into his psychiatric disorder, and he does not believe he has schizophrenia. Isaac also does not like having to take medications, partly because of the weight gain he has experienced from his antipsychotic medication. He periodically stops taking his medications when he feels better, which often leads to relapses in his symptoms, a deterioration in functioning, and sometimes rehospitalization.

HISTORY

Isaac first began to experience psychiatric problems 10 years ago. During the summer before his junior year in college, he was working in a busy office. He became increasingly concerned that his officemates were "out to get him" and that there was an intricate plot to discredit him. He also believed that his coworkers were secretly communicating with each other about him through certain facial expressions, choice of clothing, and the configuration of items on their desks. As his paranoia escalated, he became more disorganized in his thinking and behavior, he was less able to take care of his daily activities, and he experienced increased difficulties performing his job because of a combination of difficulties with attention and fear of his co-workers, and he eventually stopped coming to work. Isaac began to believe he was dying and attributed a variety of factors that were playing a role in his demise, including being poisoned by indoor air pollution. Isaac moved back home with his parents and informed them that he would not be returning to school in the fall. As a result of Isaac's symptoms, combined with the deterioration in his ability to take care of himself and meet role expectations at work and school, his parents took him to a mental health professional, who arranged for him to be hospitalized due to the extent of his functional impairment.

During this hospitalization, Isaac was first diagnosed with provisional schizophreniform disorder and treated with antipsychotic medication. Isaac benefited from his treatment, and his most flagrant symptoms improved substantially, including his belief that others were plotting against him. He was discharged after a 4-week period and referred to his local community mental health center for follow-up treatment and rehabilitation. Although Isaac's symptoms were improved, he continued to have impairments in his functioning, including his self-care skills, limited social relationships, and decreased ability to work or attend school in his previous capacity. When these impairments in psychosocial functioning had persisted for 6 months, his diagnosis was changed to schizophrenia.

Although Isaac continued to have symptoms and impairments of schizophrenia since he first developed the disorder 10 years ago, he also made some positive steps toward improving the quality of his life, with the help of his treatment team and his family. After several years of living at home, Isaac moved out 2 years ago to his own apartment. Isaac has been able to live on his own with the support of his family members and his case manager, who coordinates his care with Isaac's treatment team. At first when Isaac moved back home, there was a significant amount of tension in the household, as his parents and younger sister did not understand the nature of his illness and were upset by his occasionally disruptive living habits, such as staying up much of the night. With the help of a clinician who worked with Isaac and his family for 15 months after he returned home, his family was able to learn more about schizophrenia, the principles of its treatment, and strategies for solving problems together.

Last, after attending a local day treatment program, Isaac became interested in working. The mental health center where he receives his treatment had a supported employment program in which an employment specialist was assigned to Isaac to help him find a job in his area of interest and to provide supports to help him keep that job. Isaac said that he was interested in working with animals, so his employment specialist helped him get a part-time job at a local pet store, where he cares for the

animals, feeds them, and cleans their cages. Isaac has kept this job for almost 2 years; on two occasions he has had to take some time off when he had a relapse of his symptoms and had to return to the hospital. Isaac's employment specialist arranged with his employer for him to be able to return to his job when he had recovered from his relapse. Isaac's case manager and employment specialist also worked together to motivate Isaac to participate in a program designed to teach him more about his psychiatric disorder and how to manage it in collaboration with others, in order to achieve his recovery goal of returning to school and completing his college degree.

Assessment

A diagnosis of schizophrenia was confirmed using the Structured Interview for *DSM* (SCID). Many of the symptoms described in this vignette are highlighted in *DSM-5* criteria for schizophrenia. Regarding the A criteria, Isaac clearly experienced three "characteristic symptoms, " including delusions (e.g., his beliefs about his coworkers and being poisoned by air pollution), disorganized speech and behavior, and negative symptoms (e.g., flattened affect, apathy). In terms of the B criteria, Isaac has experienced clear impairments in his social and occupational functioning—at the time of diagnosis, he was no longer able to care for himself or go to work, and he had dropped out of school. The duration criteria of *DSM-5* were met because these difficulties lasted longer than 6 months. In addition, with respect to the D and E diagnostic criteria for schizophrenia, other diagnoses were ruled out (e.g., mood disorders, substance abuse, developmental disorders). In addition to illustrating some of the symptoms and characteristic impairments of schizophrenia, this vignette illustrates that people with this illness are often able to lead rewarding and productive lives, usually with the help of pharmacological and psychological treatment, as well as social supports, despite continued symptoms and impairment due to the illness.

SUMMARY

Schizophrenia is a severe, long-term psychiatric illness characterized by impairments in social functioning, the ability to work, self-care skills, positive symptoms (hallucinations, delusions), negative symptoms (social withdrawal, apathy), and cognitive impairments. Schizophrenia is a relatively common illness, afflicting approximately 1% of the population, and tends to have an episodic course over the lifetime, with symptoms gradually improving over the long term. Most evidence indicates that schizophrenia is a biological illness that may be caused by a variety of factors, such as genetic contributions and early environmental influences (e.g., insults to the developing fetus).

Despite the biological nature of schizophrenia, environmental stress can either precipitate the onset of the illness or symptom relapses. Schizophrenia can be reliably diagnosed with structured clinical interviews, with particular attention paid to the differential diagnosis of affective disorders. There is a high comorbidity of substance use disorders in persons with schizophrenia, which must be treated if positive outcomes are to accrue. Psychological assessment of schizophrenia is most useful when it focuses on behavioral, rather than dynamic, dimensions of the illness. Thus,

assessments and interventions focused on social skill deficits and family functioning have yielded promising treatment results. Biological assessments are useful at this time primarily for descriptive rather than clinical purposes. Finally, there are a great many issues related to gender and racial or ethnic factors that remain unexplored.

Although schizophrenia remains one of the most challenging psychiatric illnesses to treat, substantial advances have been made in recent years in developing reliable diagnostic systems, understanding the role of various etiological factors, development of effective pharmacological and psychosocial treatments, and the identification of factors that mediate the long-term outcome of the illness, such as stress and substance abuse. These developments bode well for the ability of researchers and clinicians to continue to make headway in treating this serious illness.

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CHAPTER 6

Bipolar and Related Disorders

DAVID J. MIKLOWITZ and SHERI L. JOHNSON

Over the past two decades, there has been a considerable resurgence of interest in bipolar disorder (BD; formerly known as manic-depressive illness). This resurgence is attributable in part to the availability of new pharmacological agents, disorder-specific psychosocial treatments, and data on genetic mechanisms and neurophysiological and neuroanatomical correlates. It has also been driven by the increasing recognition that the onset of the disorder is often in childhood or adolescence.

In this chapter we describe the disorder from the vantage points of diagnostic criteria, diagnostic controversies, epidemiology, and course and prognosis, with particular attention to developmental considerations pertinent to early-onset bipolar illness. A case study illustrates these issues.

We discuss the etiology and prognosis of BD from both a genetic and a psychosocial viewpoint. Current etiological models view bipolar disorder as a primarily genetic illness whose onset can be elicited by environmental stressors, although the nature of the inherited biological vulnerability is unclear. Although few studies have examined psychosocial stressors relevant to the onset of bipolar disorder, there is now a considerable literature on psychosocial stressors that affect the course and outcome of the disease. In the final sections, we summarize the major recent findings concerning the treatment of the disorder and offer directions for further research.

DESCRIPTION OF THE DISORDER

The core symptoms believed to constitute bipolar mania—elation, grandiosity, and hyperactivation—have not fundamentally changed from one edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*) to the next. In this section, we describe the core features of mania/hypomania and depression and provide an update on the rules of classification according to *DSM-5* (American Psychiatric Association [APA], 2013).

Manic, Hypomanic, Depressive, and Mixed Episodes

Bipolar disorder (BD) is defined by manic symptoms. According to the *DSM-5*(APA, 2013), people with bipolar, manic episodes experience elated, expansive, or irritable mood (or any combination of these) and increased activity, plus at least three (four if the mood is only irritable) of the following symptoms: decreased need for sleep; racing thoughts or flight of ideas; rapid speech; inflated self-esteem (also called grandiosity); impulsive, reckless behavior (e.g., spending sprees, hypersexuality); and distractibility. These symptoms must be present for at least 1 week or interrupted by hospitalization or emergency treatment. They must also cause functional impairment. Hypomania is characterized by parallel symptoms, but the criteria specify only that the symptoms last at least 4 days and result in a distinct, observable change in functioning rather than severe impairment. Although persons with bipolar disorder often experience both depression and mania, a person who has only had one lifetime manic episode and no depression is still diagnosed with bipolar I disorder.

DSM-5 criteria differ from *DSM-IV-TR* (APA, 2000) in listing increased activity as one of the cardinal symptoms of mania and hypomania. It has been argued that changes in activity may be more easily recognized than changes in subjective mood state. As such, it is hoped that the *DSM-5* criteria may provide for better accuracy and reliability in the detection of manic and hypomanic episodes.

Depressive episodes, when present, last for at least 2 weeks and are characterized by at least five symptoms, of which sad mood or loss of interest or pleasure in daily activities must be one (criterion A symptoms), plus insomnia or hypersomnia, psychomotor agitation or retardation, increases or decreases in weight or appetite, loss of energy, difficulty concentrating or making decisions, feelings of worthlessness, and suicidal ideation or behavior (criterion B symptoms). Depression must also be associated with functional impairment. Manic or depressive episodes that are clearly related to an ingested substance or to biological treatments—including antidepressant medications—are classified as substance-induced mood disorders.

A major change in the *DSM-5* is the classification of episodes in which manic and depressive symptoms occur simultaneously—what used to be called a mixed episode. The *DSM-5* refers to mixed features as a course specifier that can occur in mania or depression, whether of the unipolar or bipolar variety. A patient with mania has mixed features if he or she has three co-occurring symptoms of depression. If he or she has major depressive disorder, the mixed specifier is met by having three simultaneous manic or hypomanic symptoms. Thus, a manic patient meets the mixed specifier criteria if he or she has irritable mood, increased activity, decreased need for sleep, impulsive behavior, grandiosity, and pressure of speech (all manic symptoms) along with loss of interests, suicidal thinking, and feelings of worthlessness (depressive symptoms). The new criteria, although more complicated than those in the *DSM-IV*, are intended to match what clinicians see in practice.

Bipolar Subtypes

Bipolar I disorder is defined by the presence of a single manic episode that is not substance-induced (see the following case study). In other words, patients need not

have experienced a major depressive episode to be called bipolar I. Rates of unipolar mania are between 25% and 33% in community samples but only about 10% in clinical samples (Depue & Monroe, 1978; Karkowski & Kendler, 1997; Kessler, Chiu, Demler, & Walters, 2005; Weissman & Myers, 1978). There is some evidence, however, that most patients with unipolar mania eventually develop depressive episodes. In a 20-year study of unipolar mania, 20 of 27 patients had episodes of depression during the follow-up period (Solomon et al., 2003).

Bipolar II disorder is characterized by major depressive episodes alternating with hypomanic episodes. Both must be present; one cannot be diagnosed with bipolar II disorder on the basis of hypomanic episodes alone. About 1 in 10 bipolar II patients eventually develops a full manic or mixed episode over a 10-year follow-up, and, thus, converts to bipolar I disorder (Coryell et al., 1995).

Cyclothymia is a variant of bipolar disorder characterized by 2 or more years (or 1 year among adolescents) of alternations between hypomanic and depressive symptoms, but none of these alternations meet the full *DSM-5* criteria for a hypomanic or major depressive episode. Bipolar disorder, not elsewhere classified (previously "not otherwise specified") is reserved for patients whose disorder meets the minimum number of required symptoms but not the duration requirements for a full manic, hypomanic, or depressive, episode. Many childhood-onset patients receive this subthreshold diagnosis, and up to 50% "convert" to bipolar I or II disorder over 5 years (Axelson, Birmaher, Strober, et al., 2011).

EPIDEMIOLOGY

Differences in epidemiological estimates vary across studies, depending in part on culture and on how broadly the bipolar spectrum is defined.

A multinational study conducted by the World Health Organization reported lifetime prevalence rates in 61,392 adults in 11 countries: 0.6% for bipolar I disorder, 0.4% for bipolar II disorder, and 1.4% for subthreshold bipolar disorder. The highest rates were observed in the United States; lifetime prevalence rates were 1.0% for bipolar I disorders, 1.1% for bipolar II, and 2.4% for "subthreshold" BD (Merikangas et al., 2007). Although there are fewer epidemiological data on cyclothymic disorder, it is believed to affect as much as 4.2% of the general population (Regeer et al., 2004).

Age at Onset

The onset of mood disorders appears to be getting younger in successive birth cohorts (Kessler et al., 2005; Wickramaratne, Weissman, Leaf, & Holford, 1989). Kessler et al. (2005) reported that the lifetime risk of bipolar I or II disorders in 18- to 29-year-olds was 22 times higher than in persons over 60. It is possible, however, that younger persons feel less stigmatized by psychiatric symptoms and are more likely than older persons to report mood disorder (notably manic) symptoms.

In a large (N = 10,123) community sample of adolescents in the United States, 2.5% met lifetime *DSM-IV* criteria for bipolar I or II disorder (Merikangas et al.,

2012). Although many investigators suspect that bipolar disorder is more likely to be diagnosed by practitioners in U.S. children (e.g., Reichart & Nolen, 2004), the base rates of the disorder appear comparable across countries when standardized diagnostic interviews are used. An aggregate analysis of 12 clinical studies of 16,222 children (ages 7 to 21) across the world reported a rate of bipolar spectrum disorder (1.8%) that did not significantly differ across countries (Van Meter, Moreira, & Youngstrom, 2011). The prevalence of bipolar spectrum disorders (i.e., bipolar disorder not elsewhere classified, bipolar I, and bipolar II) may be as high as 6% in U. S. treatment-seeking samples of youth (Youngstrom, Findling, Youngstrom, & Calabrese, 2005).

The mean age of onset of bipolar I disorder averages 18.2 years, and 20.3 years for bipolar II (Merikangas et al., 2007), but there is substantial variability. Between 50% and 67% of patients develop the disease by age 18, and between 15% and 28% before age 13 (Perlis et al., 2004). Earlier age at onset is associated with rapid cycling and other negative outcomes in adulthood (Coryell et al., 2003; Schneck et al., 2004).

GENDER AND RACIAL-ETHNIC ISSUES

Women and men are equally likely to develop bipolar I disorder. Women, however, report more depressive episodes than men and, correspondingly, are more likely to be diagnosed with bipolar II disorder (e.g., Leibenluft, 1997; Schneck et al., 2004). Women are also more likely to meet experience rapid-cycling BD (at least four episodes per year), again potentially related to the greater vulnerability to depression (Schneck et al., 2004).

Less is known about racial and ethnic differences in the diagnosis and treatment of BD. In the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), African American and Latino patients received fewer prescriptions for psychiatric medications than European American patients (Gonzalez et al., 2007). Moreover, African American bipolar patients were less likely than Caucasian patients to have an outpatient follow-up visit within 3 months of the initial diagnosis (Kilbourne et al., 2005).

Evidence suggests major racial disparities in the treatment of bipolar disorder. In the NCS-R major epidemiological study, none of the African American persons who were diagnosed with bipolar disorder were receiving adequate treatment (Johnson & Johnson, 2014). One study found that adult African American patients were less likely than Caucasians to be prescribed mood stabilizers or benzodiazepines and more likely to have been given antipsychotic medications (Kupfer, Frank, Grochocinski, Houck, & Brown, 2005). African American adolescents with bipolar disorder are treated for longer periods than Caucasian adolescents with atypical antipsychotics, even after adjusting for the severity of psychotic symptoms (Patel, DelBello, Keck, & Strakowski, 2005). Not surprisingly given the treatment deficits, the course of BD illness may be worse among African American patients, who are more likely to have attempted suicide and been hospitalized than Caucasian patients. The reasons for these racial disparities in treatment are unclear, but are not explained by lack of insurance, lack of treatment-seeking, or lack of acknowledgment of symptoms among African American patients (Johnson & Johnson, 2014).

CLINICAL PICTURE

Recent studies have examined the factor structure of the manic syndrome. A principal component analysis of data from 576 diagnosed manic patients identified seven stable underlying factors: depressive mood, irritable aggression, insomnia, depressive inhibition, pure manic symptoms, emotional lability/agitation, and psychosis (Sato, Bottlender, Kleindienst, & Moller, 2002). Through cluster analysis, Sato et al. identified four phenomenological subtypes of acute mania: pure, aggressive, psychotic, and depressive-mixed mania.

The pattern of manic symptoms has been investigated in youths with bipolar disorder. A meta-analysis of seven studies examining the phenomenological characteristics of mania among children and adolescents (aged 5 to 18; Kowatch, Youngstrom, Danielyan, & Findling, 2005) found that the most common symptoms during manic episodes were increased energy, distractibility, and pressure of speech. Approximately 80% showed irritability and grandiosity, whereas 70% had the "cardinal" manic symptoms of elated mood, decreased need for sleep, or racing thoughts. Less common symptoms included hypersexuality and psychotic symptoms. Thus, most manic children showed symptoms that also characterize adult mania.

Suicide

Bipolar disorder is associated with multiple threats to health and livelihood, but the most fundamental concern is the risk of suicide. The true prevalence of suicide in BD is unclear. Early estimates suggested that rates of completed suicide in BD were 12 to 15 times higher than in the general population (Angst, Angst, Gerber-Werder, & Gamma, 2005; Harris & Barraclough, 1997; Jamison & Baldessarini, 1999) and 4 times higher than rates among patients with recurrent major depression (Brown, Beck, Steer, & Grisham, 2000). In a 44-year follow-up of patients with major depressive disorder and BD, 11% died by suicide (Angst et al., 2005). Rates are especially high among younger, recent-onset male patients and those who have comorbid alcohol or substance abuse, social isolation, depression, significant anxiety, aggression, impulsiveness, a family history of suicide, or combinations of these (Angst et al., 2005; Fawcett, Golden, & Rosenfeld, 2000; Jamison, 2000).

Some of these figures may overestimate the true suicide prevalence in BD (Bostwick & Pankratz, 2000). First, estimates based on "proportionate mortality prevalence" (percentage of the dead who died by suicide) tend to be higher than the "case fatality prevalence" (proportion of people who died by suicide). The former method is particularly error-prone for younger samples, who less commonly die from medical causes. Second, some studies base their estimates on hospitalized samples, who are at much higher risk than outpatient samples. In one study 4% of inpatients with affective disorders eventually committed suicide, compared to 2.2% of mixed inpatient/outpatient samples (Bostwick & Pankratz, 2000).

Functional Impairment

Many patients with bipolar disorder experience ongoing impairments in social, occupational, and familial functioning even between episodes, especially if they

have unresolved depressive symptoms (Altshuler et al., 2006; Fagiolini et al., 2005; Gitlin, Mintz, Sokolski, Hammen, & Altshuler, 2011). In a Stanley Foundation Network study of 253 adult patients with bipolar I or II disorder, only about one in three worked full-time outside of the home (Suppes et al., 2001). More than half (57%) were unable to work or worked only in sheltered settings. Only 42% of bipolar I, manic patients show "steady" work performance an average of 1.7 years after hospital discharge (Harrow, Goldberg, Grossman, & Meltzer, 1990). In community samples, people with bipolar disorder are at 4 times greater likelihood of work disability compared to the general population (Mitchell, Slade, & Andrews, 2004).

There is considerable variability in functional impairment, however. For example, there appears to be a link between BD and creativity or productivity: Many famous artists, musicians, writers, and politicians probably had the disorder (Jamison, 1993). Patients with bipolar disorder and highly creative persons without psychiatric disorder appear to have temperamental commonalities, such as high levels of drive, ambition, openness to new experiences and novelty seeking (Johnson, Edge, Holmes, & Carver, 2012; Nowakowska, Strong, Santosa, Wang, & Ketter, 2005). Children diagnosed with bipolar disorder and children who are the offspring of bipolar parents scored higher than healthy control children on a creativity index (Simeonova, Chang, Strong, & Ketter, 2005). Interestingly, the unaffected family members of patients with bipolar disorder demonstrate higher accomplishment and creativity than do their affected relatives.

COURSE AND PROGNOSIS

Virtually all patients with bipolar disorder have illness recurrences. The rates of recurrence, even when patients are treated with mood stabilizers, average 37% in 1 year, 60% over 2 years, and 73% over 5 years (Gitlin, Swendsen, Heller, & Hammen, 1995). Approximately one in five patients meets criteria for rapid cycling, defined by four or more distinct episodes of mania, hypomania, mixed, or depressive disorder within 1 year (Schneck et al., 2004). Biological and psychosocial factors that predict illness recurrences are discussed further in the next section.

Even more significant are the persistent, mild-to-moderate residual symptoms that most patients experience between episodes, even when undergoing pharmacotherapy (Judd et al., 2002; Keller, Lavori, Coryell, Endicott, & Mueller, 1993; Post et al., 2003). Over a 13-year follow-up, subsyndromal symptoms were present during approximately half the weeks of follow-up (Judd et al., 2002). These symptoms were predominantly depressive rather than manic. A study of children with bipolar I, II, and NOS disorders observed similar patterns of residual symptoms over a 15-month follow-up (Birmaher et al., 2009). Indeed, one of the most formidable issues in the treatment of the disorder is the stabilization of depressive symptoms (e.g., Perlis et al., 2006).

PSYCHOSOCIAL PREDICTORS OF THE COURSE OF BIPOLAR DISORDER

By the end of the 1980s, researchers began to acknowledge that biological and genetic models of BD did not explain the enormous heterogeneity in the course of the illness over time (Prien & Potter, 1990). This recognition contributed to a renewed

emphasis on psychosocial predictors in the course of the disorder. For example, Ellicott, Hammen, Gitlin, Brown, and Jamison (1990) found that BD patients with high life-events-stress scores were at 4.5 times greater risk for relapse in a 2-year follow-up than patients with medium or low life-events-stress scores. Miklowitz, Goldstein, Nuechterlein, Snyder, and Mintz (1988) found that BD I manic patients who returned after a hospitalization to families rated high on expressed emotion (EE) attitudes (criticism, hostility, or emotional overinvolvement) or who showed high levels of caregiver-to-patient affective negativity (criticism, hostility, or guilt induction) during face-to-face interactions were at high risk for relapse. Those whose families had both high EE and high affective negativity were highly likely to relapse within 9 months (94%), whereas those whose families rated low on both attributes were unlikely to relapse within this time frame (17%).

Although these first-generation studies established the prognostic role of psychosocial factors, they did not address how psychosocial variables influence depression versus mania. A second generation of research has examined which psychosocial variables influence the course of BD depression and which influence the course of mania.

Psychosocial Predictors of Depression Within Bipolar Disorder

The symptomatology and neurobiology of unipolar and BD depression have many strong parallels (Cuellar, Johnson, & Winters, 2005). Given these parallels, one might expect that psychosocial predictors of unipolar depression would influence BD depression. Here, we focus on well-established predictors of unipolar depression, including negative life events (Monroe, Harkness, Simons, & Thase, 2001), low social support (Brown & Andrews, 1986), EE (Butzlaff & Hooley, 1998), neuroticism (Gunderson, Triebwasser, Phillips, & Sullivan, 1999), and negative cognitive styles (Alloy, Reilly-Harrington, Fresco, Whitehouse, & Zechmeister, 1999).

Negative life events are perhaps the most comprehensively examined predictors of bipolar depression. Fortunately, a body of BD studies have now used interview-based measures of life events. As reviewed by Johnson (2005a), three of these cross-sectional studies found that negative life events are equally common before episodes of BD depression and unipolar depression (Malkoff-Schwartz et al., 2000; Pardoen et al., 1996; Perris, 1984). Findings of prospective studies with interview-based measures also indicate that stressful life events are correlated with slow recovery from depression (Johnson & Miller, 1997) and predict increases in BD depression over several months (Johnson et al., 2008). Thus, the most methodologically rigorous studies suggest that negative life events are precipitants of bipolar depression.

Other variables involved in unipolar depression also appear to have validity as predictors of bipolar depression. For example, neuroticism (Heerlein, Richter, Gonzalez, & Santander, 1998; Lozano & Johnson, 2001), low social support (Johnson, Winett, Meyer, Greenhouse, & Miller, 1999), family EE (Kim & Miklowitz, 2004; Yan, Hammen, Cohen, Daley, & Henry, 2004), and rejection sensitivity (Ng & Johnson, 2013) have been found to predict increases in depressive symptoms but not manic symptoms over time. Although negative cognitive styles are often documented in BD (see Cuellar et al., 2005, for review), they (a) are most likely to be

found during depression compared with well periods (Johnson & Kizer, 2002), (b) predict depression better than mania (Johnson & Fingerhut, 2004; Johnson, Meyer, Winett, & Small, 2000), and (c) can be explained by the presence of depressive history rather than manic history (Alloy et al., 1999).

In sum, variables that influence the course of unipolar depression also influence BD depression, including negative life events, poor social support, family EE, negative cognitive styles, and low self-esteem. Few studies have examined the additive or interactive effects of these risk variables in the course of BD.

Psychosocial Predictors of Mania

Compared with BD depression, less is known about the psychosocial predictors of mania. Available models highlight two sets of predictors: goal engagement and sleep/schedule disruption.

Goal Dysregulation Drawing on biological models of overly sensitive reward pathways, the goal dysregulation model suggests that people with BD may show more extreme responses to rewarding stimuli (Johnson et al., 2012). A large number of studies indicate that people with a history of mania and students who are vulnerable to mania describe themselves as more sensitive to rewards (Johnson et al., 2012). People with BD also place a stably high emphasis on goal pursuit, even when they are not in an episode (Johnson, Eisner, & Carver, 2009). This reward sensitivity would be expected to influence reactions to life events that involve major successes. Consistent with this idea, life events involving goal attainments (such as new relationships, births of children, or career successes) predict increases in manic symptoms but not depressive symptoms (Johnson et al., 2000; Johnson et al., 2008). Such effects were apparent even after controlling for baseline levels of manic symptoms and excluding life events that could have been caused by the patients' symptoms.

Why might attaining an important goal trigger manic symptoms? A set of studies suggest that for people with BD, cognition becomes much more positive during good moods than it does for other people. Available evidence suggests that mood states are associated with distinct positive shifts in confidence (Johnson et al., 2012; Stern & Berrenberg, 1979), autobiographical recall (Eich, Macaulay, & Lam, 1997), and attention to valenced stimuli (Murphy et al., 1999). Impulsivity, or the tendency to pursue rewards without awareness of potential negative consequences, also becomes elevated as people become manic (Swann, Dougherty, Pazzaglia, Pham, & Moeller, 2004) or even more mildly happy (Muhtadie, Johnson, Carver, Gotlib, & Ketter, 2014). Mood-state-dependent shifts in confidence may contribute to increased goal setting (Johnson, 2005b). In turn, investment in goal pursuit predicts increases in manic symptoms over several months (Lozano & Johnson, 2001). Consistent with these findings, experience sampling data suggest that goal attainments trigger increased goal engagement for those with bipolar disorder (Fulford, Johnson, Llabre, & Carver, 2010), which, in turn, may trigger manic symptoms (Johnson, Carver, & Gotlib, 2012).

Reward engages confidence and goal pursuit but may also bring to mind memories of failure or feelings of low self-worth (Eisner, Johnson, & Carver, 2008). In one study

(Miklowitz, Alatiq, Geddes, Goodwin, & Williams, 2010), remitted or partially remitted patients with BD, patients with MDD, and healthy controls unscrambled six-word strings into five-word sentences, leaving out one word. The extra word allowed the sentences to be completed in a negative, neutral, or "hyperpositive" (manic/goal-oriented) way. Under conditions of reward (a pleasing bell tone for every four sentences completed), all subjects completed more sentences than in the non-reward conditions. However, patients with BD unscrambled more negative sentences under conditions of reward than did patients with MDD. Thus, a simple reward may increase the accessibility of negative thoughts among bipolar patients, consistent with earlier notions of mania as a defense against threat or low self-esteem (Adler, 1964; Lyon, Startup, & Bentall, 1999).

Sleep and Schedule Disruption Experimental studies (Barbini et al., 1998) as well as longitudinal studies (Leibenluft, Albert, Rosenthal, & Wehr, 1996) suggest that sleep deprivation is an important trigger of manic symptoms. Wehr, Sack, and Rosenthal (1987) hypothesized that sleep disruption might be one way in which life events trigger episodes of BD, noting that illness episodes are often preceded by life events interfering with the ability to sleep (e.g., transmeridian flights, childbearing). This theory was broadened by Ehlers and colleagues (Ehlers, Frank, & Kupfer, 1988; Ehlers, Kupfer, Frank, & Monk, 1993), who suggested that social disruptions to other aspects of circadian rhythms could trigger symptoms (the "social zeitgebers model"). Consistent with this idea, Jones, Hare, and Evershed (2005) have documented that people with bipolar disorder demonstrate more variability in their daily schedules than do healthy controls. In two studies, Malkoff-Schwartz et al. (1998; 2000) found that bipolar patients reported more life events involving social-rhythm disruption (events that affect sleep or wake times, patterns of social stimulation, or daily routines) in the weeks preceding manic episodes compared to the weeks preceding depressive episodes.

Laboratory mice with mutations in "CLOCK" genes behave in ways that resemble people with mania (e.g., increases in activity, decreased sleep, reward-seeking behavior). These changes are reversed when mice are given lithium (Roybal et al., 2007). These animal models may inform the role of sleep disruptions and possibly broader schedule disruptions in the onset and course of mania.

In sum, sleep or schedule disruption is proposed to trigger manic symptoms. As with research on the predictors of bipolar depression, very few longitudinal studies of sleep disruption are available. As discussed next, some of these risk factors are amenable to modification through psychosocial intervention.

Treatment of Bipolar Disorder: Current Trends

Optimally, treatments for BD should involve combinations of pharmacological and psychosocial interventions. Unfortunately, in the era of managed care cost containment, drug treatments are often the only treatment provided. Perhaps as a result, the average duration of lithium treatment for patients in community settings is only 76 days (Johnson & McFarland, 1996).

Pharmacological Treatments Distinctions are usually made between acute pharmacological treatment and maintenance treatment. The goal of acute treatment is to

stabilize an existing manic or depressive episode (for recent reviews of acute pharmacotherapy studies, see Malhi, Adams, & Berk [2009] and Geddes & Miklowitz [2013]). Adjunctive psychotherapy is usually introduced during the postepisode stabilization phase and continued throughout maintenance treatment. The goals of adjunctive psychotherapy are to minimize residual symptoms and prevent recurrences. Untreated residual symptoms of mania or depression are prospectively associated with illness recurrences (Perlis et al., 2006).

Current pharmacotherapy algorithms for mania for adult and childhood-onset patients (e.g., Kowatch, Fristad, et al., 2005; McAllister-Williams, 2006) combine mood stabilizers (e.g., lithium carbonate, divalproex sodium, carbamazepine) with atypical antipsychotic medications (e.g., olanzapine, quetiapine, risperidone, aripiprazole, ziprasidone, and less frequently, clozapine). Adjunctive antidepressant agents are often recommended for bipolar depression. When given alone, antidepressant medications can cause manic switching and acceleration of cycles in a significant number of patients (Ghaemi, Lenox, & Baldessarini, 2001). When given with mood stabilizers, however, antidepressants do not appear to cause an increase in cycling (Altshuler et al., 2003; Sachs et al., 2007). The anticonvulsant lamotrigine is an option for many patients given its antidepressant properties and lower propensity to cause cycle acceleration (Malhi et al., 2009).

Despite the clear effectiveness of many forms of pharmacotherapy, patients with BD are prone to discontinuing their medications, with as many as 60% being fully or partially noncompliant after a major episode of illness (Keck et al., 1998; Strakowski et al., 1998). Patients who discontinue their pharmacotherapy abruptly are at a high risk for recurrence and suicide attempts (Keck, McElroy, Strakowski, Bourne, & West, 1997; Suppes, Baldessarini, Faedda, Tondo, & Tohen, 1993; Tondo & Baldessarini, 2000). For example, in a naturalistic study of adolescent BD patients followed 18 months after a hospitalization, relapse was 3 times more likely among patients who discontinued lithium than among patients who remained on it. Patients describe barriers to compliance that include missing high periods, objecting to having one's moods controlled by medications, lack of information about the disorder, or lack of social or familial supports (for review, see Colom et al., 2000).

Psychotherapy as an Adjunct to Medication Maintenance Randomized controlled trials of psychotherapy indicate positive benefits for psychoeducational, skill-oriented, and interpersonal treatments. The modalities investigated in the trials have included individual, family, and group formats.

Table 6.1 lists some of the key components of empirically supported treatments for BD. Treatments supported by at least one randomized controlled trial include individual psychoeducation (Perry, Tarrier, Morriss, McCarthy, & Limb, 1999), group psychoeducation (e.g., Colom et al., 2003; Simon et al., 2005), family-focused therapy (FFT; e.g., Miklowitz, George, Richards, Simoneau, & Suddath, 2003; Rea et al., 2003), cognitive-behavioral therapy (CBT; e.g., Lam et al., 2003), and interpersonal and social rhythm therapy (IPSRT; e.g., Frank et al., 2005) (for review, see Miklowitz & Scott, 2009).

These treatments have several elements in common. First, all include an active psychoeducational component, which often involves teaching patients (and in some cases, family members) to recognize and obtain early treatment for manic episodes

Table 6.1
Key Therapeutic Elements of Psychoeducational Treatment

- Teach emotion-regulation skills when challenged by stressors.
- Encourage daily monitoring of moods and sleep cycles.
- Enhance patient's (or family members') ability to identify and intervene early with relapses.
- Track and encourage medication adherence.
- Assist patient in stabilizing sleep/wake rhythms and other daily or nightly routines.
- Educate family members about the disorder and enhance intrafamilial communication.
- Increase access to social and treatment supports.
- Help patient acquire balanced attitudes toward the self in relation to the illness.
- Encourage acceptance of the disorder.

before they develop fully. All emphasize medication adherence, avoiding alcohol and street drugs, and the use of skills to cope more effectively with stress triggers. They differ in the emphasis on specific strategies, including involvement of family members in psychoeducation (FFT), stabilizing sleep/wake rhythms (interpersonal and social rhythm therapy), and cognitive restructuring (CBT; Miklowitz, Goodwin, Bauer, & Geddes, 2008).

The treatments listed in Table 6.1 have all been found in at least one study to delay relapses of BD when combined with pharmacotherapy. The control conditions vary and have included treatment as usual, individual supportive therapy, unstructured group support, and active clinical management. There are failed replication studies as well: In a large-scale multicenter study, Scott et al. (2006) found that CBT was no more effective than treatment as usual in delaying recurrences. Post-hoc analyses, however, revealed that relative to treatment as usual, CBT was associated with longer time to recurrence among patients who had had fewer than 12 lifetime episodes, and less time to recurrence among patients with 12 or more prior episodes.

The large-scale Systematic Treatment Enhancement Program for BD (STEP-BD) attempted to examine the effects of psychosocial interventions in a practical clinical trial across 15 U.S. treatment centers (Miklowitz et al., 2007). In this trial, 293 bipolar I and II patients were randomly assigned to one of three intensive psychosocial interventions (30 sessions over 9 months of family-focused treatment, IPSRT, or CBT, or a control treatment called collaborative care [CC]). The CC involved three psychotherapy sessions over 6 weeks and focused on developing a relapse prevention plan. All patients were in an acute episode of bipolar depression at the time of randomization. All received "best practice" pharmacotherapy (i.e., mood stabilizers, atypical antipsychotic agents, or antidepressants, in various combinations) in combination with psychotherapy.

Over 1 year, being in any of the intensive psychotherapies was associated with a faster recovery from depression than being in CC. On average, patients in intensive treatment recovered within 169 days, as compared to 279 days in the CC condition. Patients in intensive treatment were also 1.6 times more likely than patients in CC to be clinically well in any given study month. Rates of recovery over 1 year were as follows: FFT, 77%; IPSRT, 65%; CBT, 60%; and CC, 52%. The differences among the three intensive modalities were not significant.

There are still many gaps in research on psychosocial treatment. For example, effect sizes for depression have been larger than those for mania prevention, and it remains unclear whether particular subgroups of patients respond more completely to individual, family, or group treatment. Few studies have identified the mechanisms of action of psychosocial interventions (for example, whether they enhance medication adherence, improve the patient's ability to recognize prodromal symptoms of recurrence, or increase insight or self-awareness).

The applicability of psychosocial interventions to early-onset BD, or children at risk for developing the illness, has begun to be investigated systematically. Several randomized trials find that family-based treatments are effective in reducing symptom severity in children with bipolar spectrum disorders (Fristad et al., 2009) and adolescents with bipolar I or II disorder (Miklowitz et al., 2008). FFT has also been found to protect against the worsening of depressive and manic symptoms in children at high genetic risk for developing bipolar disorder (Miklowitz et al., 2013).

DIAGNOSTIC CONSIDERATIONS

Although the diagnosis of BD appears straightforward by *DSM-5*, there is considerable controversy as to its diagnostic boundaries with other conditions. Possibly, conceiving of bipolar disorder as a series of dimensions may enhance the reliability of diagnoses. Here, we address controversies regarding the definition of the bipolar spectrum, diagnosis in pediatric populations, and dual diagnosis (comorbidity) considerations.

THE BIPOLAR SPECTRUM

Although it has traditionally been conceptualized as a disease involving shifts between the dramatic poles of mania and depression, there is increasing recognition that many patients have bipolar spectrum disorders, which, depending on the definition, may include subsyndromal manic episodes, manic or hypomanic episodes triggered by antidepressants, subsyndromal mixed episodes, or agitated depression (Akiskal, Benazzi, Perugi, & Rihmer, 2005; Akiskal et al., 2000). For example, Smith, Harrison, Muir, and Blackwood (2005) observed that many young adults with recurrent depression have symptoms that would be best considered within the bipolar spectrum. In a sample of young adults treated for recurrent depression at a university health service, only 16% met the *DSM-IV* criteria for bipolar disorder and 83% for recurrent major depressive illness. When broader definitions of the bipolar spectrum were used, between 47% and 77% received bipolar diagnoses. Caution is warranted in interpreting these results, as the interrater reliability of interviews designed to assess milder spectrum forms of bipolar disorder is relatively low (Kessler et al., 2006).

What is the evidence that spectrum patients are really bipolar in the classic sense? Although they do not necessarily follow the same course of illness patterns as patients with BD I or II, patients with subsyndromal forms of BD are more likely to have family histories of BD and higher rates of hypomania induced by antidepressants than people without subsyndromal BD symptoms. They also have high rates of suicide, marital disruption, and mental health service utilization compared

to those with no history of mental illness (Judd & Akiskal, 2003; Nusslock & Frank, 2011).

Some researchers have examined the bipolar spectrum as a risk factor for the development of fully syndromal BD. Assessment instruments designed to identify persons at risk include the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego—autoquestionnaire version (TEMPS-A; Akiskal et al., 2005). The TEMPS-A is a self- or parent-rated assessment of temperaments believed to precede the onset of full BD and to persist during the euthymic states. Although the TEMPS-A measures a range of mood-related symptoms and tendencies, a specific tendency toward high moods and mood variability, as captured on the cyclothymia subscale, predicted onset of BD in a 2-year follow-up of 80 children and adolescents with depression (Kochman et al., 2005).

The 79-item General Behavior Inventory (GBI; Depue, Kleinman, Davis, Hutchinson, & Krauss, 1985) evaluates lifetime experiences of depressive and manic symptoms, as well as mood variability, on 1–4 scales of frequency. High scores on the GBI during adolescence are associated with psychosocial impairment in adulthood (Klein & Depue, 1984), and a childhood version rated by parents discriminated pediatric BD from attention deficit hyperactivity disorder (ADHD; Danielson, Youngstrom, Findling, & Calabrese, 2003). Whereas the Klein et al. studies focused on the prognostic value of cyclothymic temperament, Reichart et al. (2005) found that higher scores on the GBI depression subscale were the best predictors of BD onset at 5-year follow-up among adolescents with depression.

Finally, the Hypomanic Personality Scale (Eckblad & Chapman, 1986) has been used to assess subsyndromal manic symptoms and related traits. Kwapil et al. (2000) found that high scores on this scale predicted the onset of bipolar spectrum disorders over a 13-year follow-up of a large sample of college students. Thus, self-report measures of spectrum symptoms and temperamental characteristics predict the onset of BDs in longitudinal studies.

Diagnosis in Children and Adolescents

Perhaps the most controversial diagnostic dilemma is where to draw the boundaries of the bipolar diagnosis in children. Before about 1980, belief was widespread that neither mania nor depression could occur before puberty, although individual case reports of the phenomenon existed (e.g., Anthony & Scott, 1960; Strecker, 1921). This belief has changed significantly in the past two decades (for review, see Luby & Navsaria, 2010). Unfortunately, no separate diagnostic criteria exist for juvenile BD patients, and, as a result, there is little agreement on the operational definition of a manic or mixed episode, whether well-demarcated episodes of mania and depression must occur or whether the symptoms can be chronic and unremitting, the minimum duration of episodes, and what constitutes a symptom (Biederman et al., 2003; Leibenluft, Charney, Towbin, Bhangoo, & Pine, 2003; McClellan, 2005). The reliability of the diagnosis appears to decrease with age (Meyer & Carlson, 2010).

Unfortunately, *DSM-5* has done little to improve the situation. One diagnosis, disruptive mood dysregulation disorder (DMDD), has been added to the mood disorders section to give a "diagnostic home" to children and adolescents who

have recurrent irritable outbursts as well as chronic negative affectivity. These youth have often been called bipolar in community settings. Unfortunately, the DMDD diagnosis has significant problems, such as the lack of distinction with oppositional defiant disorder, the lack of a distinctive set of associated symptoms, and few data to guide treatment (Axelson, Birmaher, Findling, et al., 2011).

One research group, led by Geller and colleagues (2002), has recommended that BD not be diagnosed in children unless elevated mood and grandiosity are present. Another group (Leibenluft et al., 2003) has recommended that BD in children be divided into three phenotypes: (1) a narrow phenotype (meets *DSM-IV* criteria for mania or hypomania with elated mood and grandiosity); (2) an intermediate phenotype (meets *DSM-IV* criteria but with irritable mood only); and (3) a broad phenotype (e.g., mania that does not meet the duration criteria for bipolar I or II or is one symptom short).

Does childhood-onset BD develop into adult BD, or are they separate conditions? The NIMH Course and Outcome of Bipolar Youth (COBY) study provides strong empirical support for one approach to phenotyping high-risk youth. This long-term prospective study showed that youth with bipolar disorder, NOS characterized by (a) one *DSM-IV* symptom less than full criteria for a manic or hypomanic episode, (b) a clear change in functioning, and (c) a minimum symptom duration of 4 hours within a day and a minimum of four lifetime episodes, were at substantially elevated risk for "converting" to BD I or II by 4- to 5-year follow-up (Birmaher et al., 2009). A family history of bipolar I or bipolar II disorder also appears important in predicting conversion rates among those with a BD-NOS profile. Among patients presenting with a BD-NOS phenotype, the risk of conversion to BD I or BD II was 52% over 4 years among those with first- or second-degree family members who had a lifetime manic episode, compared to 32% in BD-NOS patients with a negative family history for mania (Axelson, Birmaher, Strober, et al., 2011; Birmaher et al., 2009). Thus, transient manic episodes, when present in a child with a bipolar first- or second-degree relative, are a high-risk phenotype for later bipolar onset.

Another long-term study found developmental continuity for a narrow BD phenotype from late adolescence to early adulthood, but not for a broader BD phenotype marked by irritability and euphoria without the associated manic symptoms (Lewinsohn, Seeley, Buckley, & Klein, 2002). A follow-up of manic children (mean age 11) who met strict *DSM-IV* criteria revealed that 73.3% relapsed into mania over 8 years. Most importantly, youth spent 60% of the weeks in their lives with mood episodes, 40% in manic states. Between the ages of 18 and 21, 44% had a recurrence of mania and 35% had developed substance use disorders (Geller, Tillman, Bolhofner, & Zimerman, 2008).

In a reanalysis of a large-scale longitudinal study of youths in semirural parts of New York ($N = 776$, mean age 13.8), two categories of risk were defined: (1) episodic irritability (based on the parents' and child's answer to questions such as "Are there times when [the child] feels irritable or jumpy?" and "Do these times last for a week or more?") and (2) chronic irritability (persistent arguing and temper tantrums across the home and school settings). Females exhibited higher levels of episodic and chronic irritability than males. Episodic irritability was stable over time. Moreover, episodic irritability in adolescence predicted the onset of a mania by

age 16 (Leibenluft, Cohen, Gorrindo, Brook, & Pine, 2006). Episodic irritability was also a unique predictor of mania by age 22, although this relationship was mediated by the cross-sectional correlation between episodic irritability and depression in early adolescence. In contrast, chronic irritability was associated with ADHD by mid-adolescence and major depressive illness in early adulthood. Clearly, the episodicity of symptoms is an important feature to assess when attempting to distinguish risk for BD from risk for other psychiatric disorders, notably ADHD.

Dual Diagnosis

BD patients are highly likely to be diagnosed with one or more comorbid disorders. When 12-month prevalence rates in a community epidemiological sample are considered, the highest associations are found between mania/hypomania, ADHD, and anxiety disorders (e.g., Kessler et al., 2005). The prevalence of anxiety disorders in clinical and epidemiologic studies ranges from 10.6% to 62.5% for panic disorder, 7.8% to 47.2% for social anxiety disorder, 7% to 40% for post-traumatic stress disorder, 3.2% to 35% for obsessive-compulsive disorder, and 7% to 32% for generalized anxiety disorder (Simon et al., 2004). Taken together, at least some form of comorbid anxiety disorder is present for the majority of persons with bipolar disorder.

Community and clinical population studies (Brady, Casto, Lydiard, Malcolm, & Arana, 1991; Goldberg, Garno, Leon, Kocsis, & Portera, 1999; Kessler et al., 1997) have documented rates of lifetime substance use disorder ranging from 21% to 45%. This represents a sixfold increase in substance use disorders among patients with BD relative to the general population. One study found that patients were more likely to use alcohol during depressive episodes and more likely to use cocaine and marijuana during manic episodes (Strakowski, DelBello, Fleck, & Arndt, 2000).

Comorbid diagnoses—and even subsyndromal symptoms of comorbid disorders—are associated with a poor prognosis of child and adult BD (Feske et al., 2000; Frank et al., 2002; Masi et al., 2004; Otto et al., 2006; Tohen, Waternaux, & Tsuang, 1990). For example, anxiety comorbidity has been linked with younger onset of BD, lower likelihood of recovery, poorer role functioning and quality of life, a greater likelihood of suicide attempts, and poorer response to medications (Henry et al., 2003; Simon et al., 2004). Studies have also documented lower recovery rates among patients with BD with a comorbid substance use disorder (Keller et al., 1986; Tohen et al., 1990) and a greater likelihood of rehospitalization (Brady et al., 1991; Reich, Davies, & Himmelhoch, 1974).

A separate issue is how to distinguish BD from comorbid disorders. A case in point is ADHD. In a sample of children, Geller et al. (1998) compared the frequency of symptoms that are considered classic or pathognomonic of mania versus those typically seen in either mania or ADHD. Elated mood, grandiosity, hypersexuality, decreased need for sleep, daredevil acts, and uninhibited people-seeking were far more common in mania than ADHD. Distractibility, increased activity, and increased energy were observed in both disorders (see also Kim & Miklowitz, 2002). It has been argued that the presence of major depressive episodes among children with ADHD is a risk factor for developing BD (Chang, Steiner, & Ketter, 2000; Faraone, Biederman, Mennin, Wozniak, & Spencer, 1997;

Faraone, Biederman, Wozniak, et al., 1997; Leibenluft et al., 2006). However, long-term longitudinal studies of girls with ADHD find high rates of depression and suicidal behavior at follow-up, and low rates of BD (Hinshaw et al., 2012; Turgay & Ansari, 2006).

DIAGNOSTIC ASSESSMENT METHODS

Most patients with BD are diagnosed by a clinical interview; there are no biological tests that verify the diagnosis. The most prominent is the Structured Diagnostic Interview for *DSM-IV* (SCID; First, Spitzer, Gibbon, & Williams, 1995). Despite impressive reliability and validity statistics for bipolar I disorder, the SCID and the Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) are not sensitive in identifying the milder forms of BD (Chambers et al., 1985; Kaufman et al., 1997). For example, the SCID may underestimate identification of hypomanic episodes when comparing with diagnoses based on interviews by experienced clinicians (Dunner & Tay, 1993).

Current thinking about diagnostic assessments is that instruments like the SCID and KSADS should be supplemented by data from self-report questionnaires (especially those that examine subsyndromal forms of mania) as well as a thorough history of prior episodes involving an episode timeline, such as the National Institute of Mental Health (NIMH) Life Charting method (Leverich & Post, 1998). Life charting enables the clinician to investigate the frequency, severity, and timing of prior episodes; whether depressive, mixed, or manic episodes have dominated the clinical picture; whether other disorders (e.g., substance dependence) preceded, coincided with, or developed after the onset of the mood disorder; and to identify triggers of episodes.

ETIOLOGICAL CONSIDERATIONS

Current models of bipolar disorder are multifactorial. It is well-established that the disorder is highly heritable. The genetic and neurobiological vulnerability to bipolar disorder is believed to increase reactivity to socioenvironmental factors.

HERITABILITY

Although heritability estimates for BD have ranged from 59% to 87%, newer studies are available that estimate the prevalence of representative community samples (McGuffin et al., 2003). These studies are particularly important as they are less likely to be biased by the focus on more severe, hospitalized samples. A Finnish community-based twin sample that used structured interviews to verify diagnoses obtained a heritability estimate of 93% (Kieseppä, Partonen, Haukka, Kaprio, & Lönnqvist, 2004). A British study with a similar design yielded a heritability estimate of 85% (McGuffin et al., 2003).

The risk of BD among children of bipolar parents is 4 times greater than the risk among children of healthy parents. Children of bipolar parents, however, are also at approximately 2.7 times higher risk for developing nonaffective disorders (including

ADHD and conduct disorder) than are the children of well parents. Thus, a proportion of the familial risk is not specific to bipolar illness (Hodgins et al., 2002; LaPalme, Hodgins, & LaRoche, 1997).

Several genomic regions relevant to BD have been identified, including 13q32, 22q11, 8p22, and 10p14 (Badner & Gershon, 2002; Berrettini, 2003), but effects have generally been small and findings have not been entirely consistent from study to study (Sullivan, Daly, & O'Donovan, 2012). One model (Murray et al., 2004) emphasizes the genetic overlap between BD and schizophrenia and common susceptibility genes that predispose individuals to dopamine dysregulation and psychosis. In addition to common susceptibilities, there are probably other genes whose expression affects neurodevelopment, illness-specific neurological changes, the likelihood of exposure to certain types of environments, and the eventual outcome of BD, schizoaffective disorder, or schizophrenia (Murray et al., 2004).

Neurotransmitter Dysregulation

Increasingly, BD is being described as an "impairment of synaptic and cellular plasticity" (Manji, 2009, p. 2). This means that people with BD have genetically influenced problems with information processing in synapses and circuits (the neuronal connections between one brain structure and others).

Traditional neurotransmitter models of mood disorders have focused on norepinephrine, dopamine, and serotonin (Charney, Menkes, & Heninger, 1981; Thase, Jindal, & Howland, 2002). It is now widely believed that dysregulations in these systems interact with deficits in other neurotransmitter systems, such as gamma-aminobutyric acid (GABA) and Substance P, to produce symptoms of mood disorders (Stockmeier, 2003). Current research focuses on the functioning of neurotransmitter systems rather than on simple models of neurotransmitter levels being either high or low. Current paradigms include measuring sensitivity of the postsynaptic receptors through pharmacological challenges or neuroimaging. Molecular genetic research has also informed researchers about key neurotransmitter systems to investigate. This type of research has progressed particularly rapidly in understanding dysregulation in serotonin and dopamine systems.

Dopamine Among people without BD, several different dopamine agonists, including stimulants, have been found to trigger manic symptoms, including increases in mood, energy, and talkativeness (Willner, 1995). People with BD show pronounced behavioral effects to stimulants (Anand et al., 2000). Several paradigms have been used to challenge the dopamine system, including behavioral sensitization (the study of how repeated administration of dopamine agonists changes the sensitivity of dopaminergic reward pathways; Kalivas, Duffy, DuMars, & Skinner, 1988; Robinson & Becker, 1986) and sleep deprivation (which appears to interfere with normalizing the sensitivity of dopamine receptors; Ebert, Feistel, Barocks, Kaschka, & Pirner, 1994). Results obtained using these paradigms are consistent with the idea that BD is characterized by hypersensitivity of the dopamine system (Strakowski, Sax, Setters, & Keck, 1996; Strakowski, Sax, Setters, Stanton, & Keck, 1997). Consistent with the idea of dopamine dysfunction, a large meta-analysis

suggested a link with the A1 polymorphism of the DRD2 gene Taq IA1 (Zou et al., 2012). In animal models, a set of candidate genes for BD have been identified that relate to modulating dopamine signaling within reward pathways (Ogden et al., 2004).

Molecular genetic studies in humans have not yet identified other polymorphisms that could explain these effects. For example, BD has not been found to consistently relate to polymorphisms in the d1, d3, and d4 receptor genes or the dopamine transporter genes (Chiaroni et al., 2000; Georgieva et al., 2002; Gorwood, Bellivier, Ades, & Leboyer, 2000; Lopez et al., 2005; Manki, Kanba, Muramatsu, & Higuchi, 1996; Muglia et al., 2002).

Serotonin Neuroimaging studies indicate that mood disorders are generally associated with decreased sensitivity of the serotonin receptors (Stockmeier, 2003). The functioning of the serotonin system can also be tested by manipulating levels of tryptophan, the precursor to serotonin (Staley, Malison, & Innis, 1998). Findings of tryptophan-manipulation studies are consistent with the idea of serotonin receptor dysfunction among persons with a family history of BD (Sobczak, Honig, Schmitt, & Riedel, 2003; Sobczak et al., 2002). Meta-analyses of the more than 20 studies of the serotonin transporter region in BD have yielded positive but small effects (e.g., Cho et al., 2005; Lasky-Su, Faraone, Glatt, & Tsuang, 2005). Unfortunately, studies to date have not examined interactions of the serotonin transporter gene with environmental risk in predicting vulnerability to BD.

BRAIN REGIONS INVOLVED IN BIPOLAR DISORDER

Although findings are not entirely consistent, neuroimaging studies implicate a set of structures in the pathophysiology of BD. Many of these regions overlap substantially with those involved in emotional reactivity and regulation, and as such, many parallels are present with the brain correlates of unipolar depression (Davidson, Pizzagalli, & Nitschke, 2002; Mayberg, Keightley, Mahurin, & Brannan, 2004). Differences between bipolar and unipolar depression are also found (Delvecchio et al., 2012). Key structures relevant to bipolar disorder include the amygdala, which is involved in the detection of the significance of emotionally salient stimuli; regions involved in effective cognitive regulation of emotions and goal pursuit, such as regions of the prefrontal cortex, anterior cingulate, and hippocampus; and structures relevant to reward sensitivity (e.g., basal ganglia). One model suggests that mood disorders are characterized by increased activity in regions involved in emotional sensitivity, combined with diminished activity in regions involved in effective thinking and planning in response to emotional cues (Phillips, Drevets, Rauch, & Lane, 2003).

More specifically, several Positron Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI) studies of neural activity during cognitive or emotional tasks have shown a pattern of amygdala hyperactivity among people with bipolar I disorder (Altshuler, Bookheimer, Proenza, et al., 2005; Chang et al., 2004; Kruger, Seminowicz, Goldapple, Kennedy, & Mayberg, 2003; Lawrence et al., 2004). Some adult studies correspondingly suggest above-average volume of the amygdala (Phillips et al., 2003).

People with BD also appear to demonstrate diminished activity of the hippocampus and some regions of the prefrontal cortex (Kruger et al., 2003). In parallel with the findings of functional studies, structural studies have found that BD is associated with a smaller-than-average volume in the prefrontal cortex, basal ganglia, hippocampus, and anterior cingulate (Phillips et al., 2003). Findings regarding diminished volume of the hippocampus have been identified in juvenile BD (Frazier et al., 2005). Diminished function of the prefrontal cortex and related circuits might interfere with effective planning and goal pursuit in the context of emotion, leading to a low capacity to regulate emotion. Although prefrontal cortical deficits have been implicated in schizophrenia as well (Barch, 2005), recent research suggests that the prefrontal deficits in BD compared to schizophrenia may be more specific to the orbitofrontal cortex (Altshuler, Bookheimer, Townsend, et al., 2005; Cotter, Hudson, & Landau, 2005). Several recent studies have suggested diminished connectivity of regions of the prefrontal cortex with the amygdala when persons with bipolar disorder are viewing positive stimuli, although findings have not been congruent regarding which regions of the prefrontal cortex are implicated (Almeida et al., 2009; Versace et al., 2010; Wang et al., 2009).

Patterns of neural activation appear to shift with mood episodes. During depression, diminished activity in the anterior cingulate is observed (Mayberg et al., 2004). During mania, persons with BD may show diminished reactivity to negative stimuli compared with healthy or euthymic persons. For example, after viewing faces with different negative emotional expressions, patients with mania showed decreases in amygdala and subgenual anterior cingulate cortex activity compared to controls (Lennox, Jacob, Calder, Lupson, & Bullmore, 2004). Hence, brain regions involved in identifying the importance of negative stimuli appear to become less active during manic episodes.

Finally, given models of reward sensitivity in BD, the role of structures within the basal ganglia, including the nucleus accumbens (Knutson, Adams, Fong, & Hommer, 2001), has become an important focus of research. Both at rest and during motor tasks, the level of activity in the basal ganglia is positively correlated with the concurrent level of manic symptoms (Blumberg et al., 1999; Caligiuri et al., 2003; Delvecchio et al., 2012).

Hence, one theory is that BD is related to dysregulation in brain regions relevant to emotional reactivity, such as the amygdala, as well as regions in the prefrontal cortex involved in the regulation of emotion and cognitive control. Much of this research demonstrates strong parallels with unipolar depression. Evidence suggests that neural activation is somewhat mood-state dependent. Regions involved in reward motivation are an important focus for research.

CASE STUDY

Case Identification and Presenting Complaints

Leonard, a 57-year-old White male, lived with his wife, Helen, and 15-year-old son in a rented house in the suburbs of a major metropolitan area. His wife requested treatment because of his angry outbursts, sleep disturbance, and bizarre

preoccupations. He had become preoccupied with kickboxing and was spending hours on the Internet examining relevant websites and writing about it. She discovered that he had written a 500-page manuscript describing the mechanics of kickboxing, containing sections that were rambling, philosophical, and at times incoherent. She explained that he was frequently awake until 4 A.M. and went to bed smelling of alcohol. For nearly 5 years he had been unable to hold a job.

Leonard presented in his first interview as combative and oppositional. He admitted that he had been feeling "revved" over the past 2 weeks, that he felt full of energy and ideas, and that he needed little sleep, but he denied any negative effects of his symptoms. He described an incident that appeared to be related to his recent manic behavior. He had made contact with a kickboxing champion in another state and had started writing to this man about setting up a new television network devoted to kickboxing. He also claimed he was going to start his own studio. The plans seemed unrealistic given that he had little formal training in this sport and had no money to rent a studio. The kickboxing champion had stopped responding to Leonard's emails, which, Leonard claimed, might be because "he's raising money and wants to surprise me."

Leonard had one manic episode accompanied by hospitalization when he was in college. He had become entranced by a female professor and believed that she was related to him by blood. He began calling her continually and finally followed her out to a parking lot and tried to block her from getting into her car. A passerby called the police, and Leonard was taken to the hospital. He was admitted with the diagnosis of bipolar I, manic episode.

Since this time Leonard had functioned poorly. His work had been intermittent, and he had been fired several times because, as he explained, "My bosses are always idiots and I'm more than happy to tell them so." He had tried to set up a web-based business selling automobile window shields but had made little money. He met Helen during a hiking excursion for singles. They had married approximately 1 year after they met (a period of relative stability for Leonard) and had a child 1 year later.

Leonard had begun medication shortly after his son was born, explaining that he wanted to become a stable father. His psychiatrist recommended lithium carbonate 1,200 mg and divalproex sodium (Depakote) at 2,000 mg. Although Leonard did not have further manic episodes, he had several hypomanic periods and complained of an ongoing depression that never fully remitted. He had thought of suicide several times, and these fantasies usually had a dramatic quality. For example, he fantasized about setting himself on fire and then jumping from a tall building. He never made an attempt.

The clinician who evaluated Leonard administered the Structured Clinical Interview for *DSM-IV* (First et al., 1995), which involved an individual interview with him, followed by a separate interview with his wife. The interview confirmed the presence of elated and irritable mood for the past 2 weeks, along with inflated self-esteem, increased activity, decreased need for sleep, flight of ideas and racing thoughts, pressure of speech, and increased spending. His behavior did not require hospitalization but clearly interfered with his functioning. He was given a diagnosis of bipolar disorder I, manic episode and started on a regimen of lithium, divalproex, and an atypical antipsychotic agent, quetiapine (Seroquel).

SUMMARY

Much progress has been made in clarifying the diagnostic boundaries, genetic pathways, and neurobiological mechanisms relevant to bipolar illness. New studies recognize the strong influence of psychosocial variables against this background of biological and genetic vulnerability. Psychotherapy is an effective adjunct to pharmacotherapy in the long-term maintenance treatment of the illness, notably interventions that focus on enhancing the patient's understanding of the disorder and effectiveness in coping with its cycling.

Major focal areas for future studies include clarifying the validity of the bipolar spectrum. It is unclear whether bipolar illness should include only *DSM-5*-defined bipolar I or bipolar II disorder or whether it should also include subsyndromal mixed presentations (e.g., depression with significant anxious-agitation), cyclothymia, or episodes of mania, hypomania, or depression that do not meet the full severity or duration criteria. Nowhere are these questions more critical than in defining childhood-onset BD, which is being diagnosed with increasing frequency. In the future, it may be that fMRI or other imaging techniques will identify brain changes uniquely associated with bipolar illness, but until that time we must rely on clinical interviews and supplemental questionnaires to diagnose these conditions. Research that improves the reliability, clinical utility, and consumer acceptance of existing diagnostic methods is therefore critical.

The interface between psychosocial and biological risk factors deserves considerable study, especially as these factors relate to different poles of the disorder. As we have summarized, life events involving goal attainment and factors that disrupt sleep are strongly correlated with the onset of manic episodes, although their role in predicting illness onset has not been established in longitudinal studies. High intrafamilial EE and negative life events stress are most consistently associated with depressive episodes. Laboratory-based translational research may help clarify the avenues from specific stressors to biological changes to manic versus depressive symptom exacerbations.

The optimal combinations of psychotherapy and pharmacotherapy must be identified in trials that sample populations of diverse ethnicity, socioeconomic status, psychiatric and medical comorbidity, and chronicity. Large-scale studies such as STEP-BD are a move in this direction, but even studies of this size can be underpowered for examining treatment effects within specific subgroups (e.g., patients with comorbid substance dependence, rapid-cycling patients, patients of African American or Latino heritage). Studies that adapt treatment methods to the cultural needs of specific populations are essential to moving the field forward.

Last, treatment studies should consider the synergy between biological and psychosocial interventions, and under what conditions combining one with the other will produce the most enduring effects. For example, drugs that stabilize mood symptoms may also energize patients to the extent that they become more amenable to the skill-oriented tasks of cognitive-behavioral treatment. Psychoeducational treatments may increase medication adherence, which in turn may allow patients to remain stable on fewer medications or on lower dosages. Interpersonal or family interventions that increase the patient's ability to benefit from social support and decrease the impact of family or life stressors may decrease the need for adjunctive

antidepressants in long-term maintenance. Ideally, the next generation of clinical research in BD will address these questions.

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CHAPTER 7

Mood Disorders: Depressive Disorders

LEILANI FELICIANO and BRENNA N. RENN

DESCRIPTION OF THE DISORDER

Depressive disorders are among the most common psychiatric disorders occurring in adulthood (Waraich, Goldner, Somers, & Hsu, 2004). They are characterized by feelings of sadness, lack of interest in formerly enjoyable pursuits, sleep and appetite disturbances, feelings of worthlessness, and at times thoughts of death and dying. In older adults, depressive disorders may present differently, with less reported sadness and depression and more somatic complaints (Hybels, Blazer, Pieper, Landerman, & Steffens, 2009).

All depressive disorders are extremely debilitating and negatively impact the quality of life of those afflicted. At the beginning of this millennium, depressive disorders were second only to heart disease as the illness most responsible for poor quality of life and disability (Pincus & Pettit, 2001). By the year 2030, major depressive disorder (MDD) is predicted to be among the leading causes of disability globally, comparable to heart disease and second only to HIV/AIDS (Mathers & Loncar, 2006). Depression is also associated with increased suicide risk. In a recent cross-national sample of 17 countries, individuals with a mood disorder had an odds ratio of 3.4 to 5.9 over that of individuals without a mood disorder, even after controlling for such factors as age, education, and relationship status (Nock et al., 2008). In terms of suicide completion, early statistics indicated that 15% of people with major depression completed suicide (Guze & Robins, 1970), although recent estimates are more conservative and place the lifetime risk of completed suicide between 2.2% (Bostwick & Pankratz, 2000) and 4.2% (Coryell & Young, 2005) in individuals with depressive disorders. Comorbid substance use and personality disorders (borderline personality disorder in particular) increase the risk of attempted and completed suicide in people with depressive disorders (Bolton, Pagura, Enns, Grant, & Sareen, 2010). Fortunately, depressive disorders can be treated successfully with psychotherapy, antidepressant medication, or both (Norman & Burrows, 2007).

The research on these disorders continues to grow, and we know quite a bit about how depressive disorders are presented, their etiology, and their course and prognosis. The purpose of this chapter is to describe the depressive disorders and the revised

diagnostic criteria, discuss their prevalence and effects on people who have these disorders, examine the best methods for assessing depressive disorders, and present the latest research on their etiology.

Diagnosis and Description

According to the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*; American Psychiatric Association [APA], 2013), depressive disorders now include several categories of illnesses: disruptive mood dysregulation disorder (applicable to children up to age 18 only), major depressive disorder (MDD), persistent depressive disorder (formerly dysthymic disorder), premenstrual dysphoric disorder, substance/medication-induced depressive disorder, and depressive disorder due to a medical condition. The previous catchall category Depressive Disorder Not Otherwise Specified (Depression NOS) has been replaced with a choice of other specified depressive disorder and unspecified depressive disorder, which allows for more clinical specificity. Using three of the diagnostic categories as an example, Table 7.1 illustrates how mood disorders in adulthood share common symptoms and clinical features. First, all disorders consist of mood symptoms, which include feeling "sad, empty, or irritable." Second, these disorders are characterized by vegetative symptoms, which include fatigue, social withdrawal, and agitation. As with all mental

Table 7.1
Sample Diagnostic Criteria

Symptoms	Major Depressive Disorder	Persistent Depressive Disorder (previously Dysthymic Disorder)	Other Specified Depressive Disorder (previously Depression NOS)
Depression	Either depressed mood or anhedonia along with at least four other symptoms must be present for no less than 2 weeks, all day nearly every day.	Depressed mood, plus two or more symptoms must be present for at least 2 years, occurring more days than not.	Either depression or anhedonia plus other symptoms specific to disorder specified. Duration is variable depending on disorder specified.
Anhedonia			
Change in appetite			
Change in sleep			
Agitation or slowing			
Loss of energy			
Decreased concentration/ trouble making decisions			
Thoughts of death/suicide			
Feeling guilty or worthless			

disorders, these symptoms must cause significant distress and affect the person's functioning.

Disturbances in sleep and appetite are also common, with lack of sleep and appetite being more typical with depression, although patients with an atypical presentation (discussed later) will complain of hypersomnia (increased sleep) or weight gain caused by frequent eating/overeating. Finally, all disorders consist of cognitive symptoms. These include trouble concentrating; difficulty making decisions; low self-esteem; negative thoughts about oneself, the world, and others; guilt; and suicidal ideation. The degree to which these features occur and the number of symptoms present will determine which type of depressive disorder a person may be experiencing. Next we discuss each mood disorder that occurs in adulthood to clarify how it can be distinguished from the others.

Major Depressive Disorder

Major depressive disorder (MDD) is the most serious and most widely studied depressive disorder. It is characterized by at least one *major depressive episode* (MDE), with no history of mania (period of intense energy, euphoria, distorted thinking, and behavioral excesses). To qualify as an MDE, either depressed mood or lack of interest or pleasure in usual activities (anhedonia) must be present, most of the day, nearly every day, and the episode must last at least 2 weeks. In addition, at least five out of nine possible symptoms (listed in Table 7.1) must be present during that same period. The symptoms must be severe enough to interfere with the individual's social, educational, or occupational functioning. Lastly, the symptom picture should not be better accounted for by another condition (e.g., a medical condition, directly related to use or withdrawal of a substance, a psychotic disorder).

Specifiers Major depressive disorder is further qualified as to its severity, chronicity, and remission status. Severity is generally determined by the degree of disability experienced by the affected person. If the person can continue to pursue obligations (work, family, and social activities), then the depression is rated as *mild*. If the person has trouble getting out of bed and can no longer engage in any obligated activities, then the depression is rated as *moderate*. If a person is thinking of death or dying; is so vegetative that he or she has not gotten out of bed, eaten, or engaged in any self-management activities, then the depression is rated as *severe*. With severe cases, if the person is exhibiting psychotic behavior, the specifier of *with psychotic features* would be designated, as well. Although it is rare, an individual with depression can exhibit symptoms of catatonia, which is characterized by immobility, excessive motor activity, extreme negativism or mutism, and bizarre posturing. In these cases, the qualifier *with catatonia* would be most appropriate. See the Diagnostic Specifiers section for more details.

A person will be diagnosed as having MDD, *recurrent type* if there has been more than one episode of MDD with a minimum period of two consecutive months (in which the person no longer qualifies for an MDE) between the episodes. Because research has found MDD to be a recurrent disorder (single episodes are rare), if a person has had an episode of MDD but is no longer experiencing any depressive symptoms, that person is considered to be *in remission*.

In addition to these qualifiers, clinicians should also note features of the disorder related to its presentation (e.g., with anxious distress, mixed features, atypical presentation) (discussed in detail later in the Diagnostic Specifiers section).

PERSISTENT DEPRESSIVE DISORDER

Persistent depressive disorder (previously Dysthymic Disorder or Dysthymia) encompasses two disorders from *DSM-IV-TR* (APA, 2000), *Chronic Major Depressive Disorder* and *Dysthymic Disorder,* and regrouped them into a single disorder. Persistent depressive disorder is generally not considered to be as severe as MDD as it requires fewer symptoms for diagnosis. However, given that the duration required for diagnosis of persistent depressive disorder is longer (2 years versus 2 weeks), the severity differential between the two diagnostic categories may be debatable.

For diagnosis, the symptoms of persistent depressive disorder (listed in Table 7.1) must be present for 2 years, during which time there should be no more than a 2-month period in which the person is symptom free. In the *DSM-IV-TR*, a diagnosis of dysthymic disorder used to carry an additional requirement that no MDE be present during the first 2 years of dysthymic disorder, although one could occur after the 2-year period. If MDD occurred after the 2-year period, it was commonly described as *double depression*. However, in the *DSM-5*, this requirement has been dropped. Thus, the criteria for an MDD may be met continuously during the 2-year span. However, because the criteria for persistent depressive disorder requires fewer symptoms, if a person ever meets full criteria for an MDE, the diagnosis should be amended to include MDD as a qualifier. In the *DSM-IV-TR*, this was previously designated as *Chronic MDD*, but in *DSM-5* this has been folded into the persistent depressive disorder category. Of course, symptoms of persistent depressive disorder must not be due exclusively to other disorders (including medical conditions) or to the direct physiological effects of a substance (including medication). As in MDD, the person must not ever have met criteria for manic episode, hypomanic episode, or cyclothymic disorder, and the disorder should not be better accounted for by any of the psychotic disorders (e.g., occur only during the course of a psychotic disorder).

Specifiers If persistent depressive disorder occurs before age 21, it is described as having *early onset*; otherwise, it is described as having *late onset*. In addition to onset qualifiers, clinicians should note the specific features of the disorder (e.g., with anxious distress, mixed features, atypical presentation, psychotic features) (discussed in the Diagnostic Specifiers section). Clinicians should also note whether the disorder has a *pure dysthymic syndrome*, where the full criteria for an MDE have never been met in the 2-year span. However, if the full criteria for an MDE have been met consistently during this 2-year span, then clinicians would specify that a *persistent MDE* was present. If there were 2-month periods within the current episode in which symptoms were subthreshold for an MDE but some depressive symptoms were present, then a specifier of *intermittent MDE, within current episode* would be given. Similarly, if intermittent MDEs have occurred previously, but not within the context of the current episode, a specifier of *intermittent MDE, without current episode* would be noted.

Premenstrual Dysphoric Disorder

Previously categorized as a provisional disorder under the *DSM-IV* (found under Appendix B, "Criteria Sets and Axes Provided for Further Study"), *premenstrual dysphoric disorder* has been instituted under the mood disorder section of *DSM-5.* This mood disorder is thought to be caused by hormonal fluctuations in the female menstrual cycle (with symptoms more severe than what is typically seen with premenstrual syndrome). The distinguishing characteristics of premenstrual dysphoric disorder include the presence of five or more mood symptoms (i.e., significant depressed mood, significant mood swings, irritability, anxiety, decreased interest in activities, difficulty concentrating, lethargy, appetite changes, sleep difficulties, feeling overwhelmed and physical symptoms) that occur in the majority of menstrual cycles (minimally over two cycles) and are tied to the course of the menstrual cycle. Thus, onset of symptoms begins during the premenstrual phase (approximately 1 week before menses), begins to remit during or shortly after menses, and is absent or minimally present in the week postmenses. As with all mood disorders, the symptoms of premenstrual dysphoric disorder are associated with significant distress and impairment in meaningful activity (e.g., negatively impacts or interferes with work, school, or social performance). The mood disturbance should not be better accounted for by another disorder (e.g., MDD, panic disorder), although it may be comorbid with other disorders.

Substance/Medication-Induced Depressive Disorder

Substance/medication-induced depressive disorder is diagnosed when an individual experiences depressed mood and/or anhedonia after exposure to a substance or medication capable of producing such effects (e.g., alcohol, hallucinogens, opioids; medications such as antiviral agents, cardiovascular agents, hormonal agents, and immunological agents, and psychotropic medications; see Botts & Ryan, 2010 for a review). This diagnosis is based on findings from the individual's history, physical examination, and/or laboratory tests that provide evidence for a temporal link between the depressive symptoms and medication/substance use or intoxication. For example, the mood disturbance should not precede the use of the substance or medication. Like other depressive disorders, symptoms of substance/medication-induced depressive disorder must be severe enough to result in clinically significant distress and/or impairment in important areas of functioning.

Although the symptoms of depression seen in this disorder may be similar to those of MDD and other depressive disorders, the disturbance seen in this diagnosis should not be better explained by another depressive disorder. Like all diagnoses, clinical judgment is essential. The clinician should evaluate whether the medication or substance is truly causative of the mood symptoms, or whether an independent depressive disorder happened to co-occur with the use of medication or substances. The symptoms of this disorder often remit within days to weeks, depending on the half-life of the substance; mood disturbances that carry this diagnosis should not persist for a substantial length of time (e.g., 1 month) after discontinuation of substance or medication use. The clinician must also rule out delirium as a cause for this mood disturbance.

Depressive Disorder Due to Another Medical Condition

In the *DSM-5,* this diagnostic category has been removed from its previous designation under Depressive Disorder, NOS and recategorized as a full depressive disorder. *Depressive disorder due to another medical condition* refers to circumstances in which depressed mood or anhedonia is present and there is clear "evidence from the history, physical examination, or laboratory findings that the disturbance is the direct pathophysiological consequence of another medical condition" (APA, 2013). That is, the clinician determines that a medical condition is present and that it is causally related to the mood disorder through a physiological pathway. For example, the clinician should evaluate the temporal relationship between any changes in the medication condition (i.e., onset, worsening, or remission) and the onset of depressive symptoms. Examples would include Depressive Disorders due to problems with the thyroid, poststroke, postsurgery, and so forth. This disorder must be distinguished from those disorders in which the symptoms are caused indirectly as when there are insufficient resources to cope with/manage the stressor (e.g., adjustment disorder with depressed mood) or are likely caused by a delirium process.

Other Specified and Unspecified Depressive Disorders

Previously in the *DSM-IV-TR*, the Depressive Disorder, Not Otherwise Specified category was treated as a catchall for depressive conditions that were provisionary and had not been studied in depth. In the *DSM-5*, this category has been phased out and replaced by two options: other specified disorder and unspecified depressive disorder.

Other Specified Disorder This category of disorders is characterized by depressive disorders that are s*ubclinical* in that they do not meet the full criteria for any of the other depressive disorders mentioned here, yet the symptoms cause significant distress or impairment in functioning. The *DSM-5* describes three examples of disorders that would fit under this category including recurrent brief depression, short-duration depressive episode, and depressive episode with insufficient symptoms, although this is not an exhaustive list. *Recurrent brief depressive disorder* is characterized by repeated episodes of depression that last for at least 2 days, but less than 2 weeks. Specifically an individual would need to present with depressed mood and at least four other symptoms for the specified time period, once per month, for 12 consecutive months in order to qualify for this diagnosis. *Short-duration depressive episode* is also characterized by depressed mood and at least four of eight symptoms of an MDE over a minimum of 4 days, but lasting less than 2 weeks. However, this diagnosis does not have the chronicity of recurrent brief depressive disorder or the severity of MDD. Lastly, *depressive episode with insufficient symptoms* requires depressed mood and at least one of eight symptoms of an MDE that persists for at least 2 weeks.

Unspecified Depressive Disorder This category is reserved for those situations in which the clinician determines that the individual's symptom presentation is characteristic of a depressive disorder (e.g., depressed mood, significant distress, or impairment in functioning), but the symptoms do not meet criteria for any other diagnostic category

of mood disorder. This category allows for clinical judgment and the flexibility of diagnosing the presence of a mood disorder when there is inadequate information available to make a differential (e.g., in short-term, integrated care settings in which there is more emphasis on solutions rather than conducting a full comprehensive intake, in emergency room settings, in situations where the individual is a poor historian and no collateral informants are available).

Diagnostic Specifiers

Clinicians add specifiers as appropriate to provide more information about an individual's unique presentation. The *DSM-5* added several new specifiers to the previous ones available under earlier editions. Specifiers can be thought of as subtypes of depressive disorders and are classified with the following: (a) anxious distress, (b) mixed features, (c) melancholic features, (d) atypical features, (e) mood-congruent psychotic features, (f) mood-incongruent psychotic features, (g) catatonia, (h) peripartum onset, and (i) seasonal pattern. *Anxious distress* may be used to describe an MDE or persistent depressive disorder characterized by psychomotor agitation such as tenseness or restless behavior, or anxious thoughts such as worry, fear, or sense of losing control. *Mixed features* refer to an MDE that presents with at least three hypomanic/manic symptoms such as expansive mood or increased psychomotor activity (e.g., decreased need for sleep, flight of ideas, pressured speech).

MDE and persistent depressive disorders can also present with *melancholic features,* such that the mood disturbance is characterized by a near-absence of the capacity for pleasure and/or an inability to feel better, even briefly, when something good happens (mood reactivity). This melancholic presentation is further classified by a sense of despondency and despair, psychomotor symptoms, early morning awakening, and depression that is worse in the morning. Some researchers have suggested that this subtype is more typically associated with biological etiology and that it may be more responsive to psychopharmacological intervention than to psychotherapies (Andrus et al., 2012; Simons & Thase, 1992).

Conversely, *atypical features* are specified during a depressive disorder in which mood reactivity is notable (i.e., the individual's mood brightens in response to something positive) and occurs in conjunction with psychomotor symptoms of weight gain or increased appetite, hypersomnia, and/or leaden paralysis (i.e., feeling as though one's limbs are heavy, leaden, or weighed down). These individuals may also present with a long-standing pattern of sensitivity to "interpersonal rejection." This depressive subtype is thought to be primarily triggered by stressful life events or a specific psychosocial problem. Although most researchers agree there is likely to be some genetic component to this subtype as well, depression would only be expressed in the face of a major problem that a person could not solve immediately (e.g., loss of employment). This tends to be interpreted as suggesting a depressive disorder that is more likely to respond to psychosocial interventions than to medications (Nutt et al., 2010).

Specifiers related to *psychotic features* provide information about whether the depressive disorder presents with delusions and/or hallucinations, and whether these symptoms are *congruent* or *incongruent* with depressed mood (i.e., content of hallucinations and/or delusions involve depressive themes such as disease, death,

punishment, or guilt). If catatonic features occur during an MDE, the *catatonia* specifier is used to describe this marked decrease in reactivity to the environment. Although historically associated with schizophrenia, catatonia can occur in other disorders, such as severe MDD.

Finally, two other specifiers provide information about mood disturbances that are related to context-specific factors. First, *peripartum onset* is specified when onset of symptoms in an MDE occurring during pregnancy (prepartum) or within the first 4 weeks following delivery (postpartum). These symptoms can occur with or without psychotic features. If an individual experiences recurrent MDEs that are temporally associated with a particular time of year (e.g., in the winter), his/her depression is specified *with seasonal pattern.*

In addition to providing more information about a context for a depressive disorder, these specifiers have clinical and prognostic utility. For example, individuals with a mixed feature presentation are at risk of receiving a bipolar disorder diagnosis in the future. Melancholic features are more frequently seen on an inpatient rather than outpatient basis and may co-occur with psychotic features. Psychotic features are associated with lower recovery rates compared to depressive episodes not complicated by psychotic presentation. Peripartum onset of an MDE with psychotic features is associated with infanticide when the mother experiences command hallucinations to kill the infant or delusions of the infant's possession.

WHEN DEPRESSION IS NOT A DEPRESSIVE DISORDER

Sometimes symptoms of depression may be present but may not be diagnosed as one of the depressive disorders. People who develop depression after a significant life stressor for a short time are more likely to be suffering from an *adjustment disorder* rather than a mood disorder (in the *DSM-5* adjustment disorders are found under the new Trauma- and Stressor-Related Disorders section). In addition, a previous manic episode will also exclude a diagnosis of MDD or persistent depressive disorder. Finally, if the individual with depression has symptoms that are better accounted for by another diagnostic category, then that diagnostic category should be assigned in lieu of a depressive disorder (e.g., schizoaffective disorder). See the section on disorders due to another psychiatric condition.

Everyone experiences feelings of sadness from time to time. This is a normal experience that should not be pathologized. Depressive symptoms are considered problematic when they persist for 2 weeks or more and are accompanied by distress and considerable difficulty managing day-to-day activities. In the next section, we provide examples of these disorders.

CLINICAL PICTURE

Major depressive disorder, dysthymic disorder, and other specified and unspecified depressive disorders all vary to a degree in their presentation but share several features that distinguish these disorders from other mental illnesses. People with depressive disorders can be identified by their pessimism and negativistic thinking, difficulty solving even everyday problems, and lack of initiative. People with

depressive disorders are also quite disabled by the illness and often report having multiple somatic symptoms.

Most people with a depressive disorder exhibit what is called *negativistic thinking*. This term was coined by Aaron Beck (Beck, 1961) and has since been used extensively to describe the cognitive style of people suffering from depressive disorders. Negativistic thinking is best described as a style of thinking that is overly pessimistic and critical. People with depression tend to expect failure and disappointment at every turn and will focus only on their past failures as a way to confirm these beliefs (Alloy et al., 2000). People with negativistic thinking also have poor self-esteem and are more likely than people without this cognitive bias to experience depressive symptoms (Verplanken, Friborg, Wang, Trafimow, & Woolf, 2007). The presence of negativistic thinking in depression is a bit of a "chicken or egg" problem: Does depression cause negativistic thinking, or does negativistic thinking cause depression? Recent research suggests that the cause of depression is more likely an imbalanced thinking style and that negativistic thinking may have a clearer association with repeated exposure to failure and disappointment. In a study by Issacowitz and Seligman (2001), people with pessimistic thinking as well as those with optimistic thinking were at risk for developing depressive symptoms after exposure to stressful life events. In fact, optimists were at higher risk for depression than pessimists were, although pessimists tended to have more persistent depression. Therefore, objective perceptions of one's abilities, of one's environment, and of other people are likely to be more protective than overly optimistic or pessimistic styles of thinking.

Negativistic thinking is primarily responsible for why individuals with depression find it difficult to engage in and enjoy activities that once gave them pleasure, and thus social isolation is a common feature of depressive disorders (Cacioppo, Hawkley, & Thisted, 2010). Many people with a depressive disorder will report that they have stopped socializing or engaging in pleasant activities, largely because they anticipate no enjoyment from the activity (Chentsova-Dutton & Hanley, 2010). As will be discussed in the section on etiology, it is felt that repeated exposure to stress will influence the reward centers of the brain; animal studies have demonstrated that repeated exposure to negative events will result in the adoption of avoidance motivation over appetitive motivation; in other words, people who experience too many negative experiences begin to anticipate that all experiences will be negative and therefore, they will be motivated by pain reduction rather than by need for pleasure (Ho & Wang, 2010).

It is important that people who have depression attempt to reengage in social activities. Increased social isolation puts the individual with depression at greater risk of severe depression. Several studies show that social support can offset the occurrence or worsening of depression, and thus increasing exposure to socialization is an important process in recovering from depression (Barros-Loscertales et al., 2010; Dichter, Felder, & Smoski, 2010; Jakupcak, Wagner, Paulson, Varra, & McFall, 2010; Mazzucchelli, Kane, & Rees, 2010).

People with a depressive disorder also tend to use passive coping skills, or they avoid solving problems (Nolen-Hoeksema, Larson, & Grayson, 1999). This is sometimes due to a preexisting skills deficit or to learned helplessness, a condition caused by repeated attempts and failures to cope with problems (Folkman & Lazarus, 1986). Most often, after people develop depression, they avoid proactive attempts to solve

problems because they anticipate that they are not capable of implementing a successful solution (Nezu, 1986). This avoidance often results in more problems; for instance, avoiding marital problems potentially results in divorce.

A relatively recent movement, *positive psychology*, focuses on an individual's strengths (virtues) as well as any skills deficits in the treatment of depression (Sin & Lyubomirsky, 2009). Seligman and Csikszentmihalyi (2000) discuss positive psychology as an adjunct to treatment of mental health problems to provide treatment to the whole person rather than a focus on treating the depressive symptoms only. The main tenets involve putting our strengths to work in achieving a balance of three lives: the pleasant life, the good life, and the meaningful life. Seligman and colleagues have designed and researched a series of Internet exercises designed to increase happiness and decrease suffering. For a more detailed review, see Seligman, Steen, Park, and Peterson (2005).

Many people are often surprised to discover how disabling depression can be. People who have depression will complain of somatic problems, such as fatigue, stomach upset, headaches, and joint pain (Viinamaeki et al., 2000). These symptoms, coupled with the pessimism and avoidant style associated with depression, are related to the increased number of disability days reported by people with depressive disorders (Pincus & Pettit, 2001). In the National Comorbidity Survey (NCS; Kessler & Frank, 1997), people with depression reported a fivefold increase in time lost from work than did those without depression. In fact, individuals treated for depression incurred greater disability costs to employers than did people needing treatment for hypertension and had costs comparable to those with more severe chronic illness like diabetes (Conti & Burton, 1995; Druss, Rosenheck, & Sledge, 2000). Data from the NCS-R (Greenberg et al., 2003) suggested that the economic burden of depression stabilized somewhat between 1990 and 2000, rising from $77.4 billion to $83.1 billion (adjusted for inflation). The majority of this burden was associated with workplace costs (e.g., lost productivity). Interestingly, costs related to treating depression are almost as great as the costs due to disability days from depression (Kessler et al., 1999), and some studies have found the treatment of depression to decrease disability days (Simon et al., 2000).

DIAGNOSTIC CONSIDERATIONS

Although the *DSM-5* provides guidelines for the diagnosis of depressive disorders, the comorbidity of other medical and psychiatric disorders can complicate a diagnostic decision. To make an accurate diagnosis of depression, the provider must consider physical health and medical history, medications, family and personal history, and psychosocial stressors. With regard to the latter, the *DSM-IV-TR* previously required that an individual with *bereavement* be excluded from an MDE diagnosis, regardless of symptom presentation, unless their symptoms lasted more than 2 months or resulted in marked impairment, suicidality, or psychotic features.

As discussed in more detail later (see Grief and Bereavement), the *DSM-5* has instituted a change in that bereavement is no longer an exclusion criteria for a diagnosis of depression; people who are suffering from the loss of a significant other could be diagnosed with a depressive disorder, if they meet the clinical characteristics of MDE (Corruble, Falissard, & Gorwood, 2011). This is not to say that bereavement

automatically results in depression; rather, this change reflects the clinical understanding that the loss of a loved one, as well as other stressful life events, can trigger a genuine mood disorder when out of proportion to a "normal" response (Kendler et al., 2003). Clinicians are urged to consider the culture of the individual in determining what is a normal or expected response to grief/loss, as grief may be expressed differently across cultures.

Medical Illness

The first important step in diagnosing depressive disorders is to have the patient get a complete physical. Depression commonly co-occurs with other mental disorders (e.g., anxiety disorders) and physical disorders (King-Kallimanis, Gum, & Kohn, 2009), which can further exacerbate distress and disability, and can challenge treatment efforts. Because many medical illnesses are related to the onset of a depressive episode, at times treating both the illness and the depression is a more efficient way to effect symptom change (Gupta, Bahadur, Gupta, & Bhugra, 2006; Katon, 2003; Simon, Von Korff, & Lin, 2005; Stover, Fenton, Rosenfeld, & Insel, 2003; Trivedi, Clayton, & Frank, 2007). For example, in endocrinological disorders like hyperthyroidism and hypothyroidism, one of the diagnostic signs is a change in affect and mood. People who are treated for these disorders experience radical changes in mood. Moreover, people with chronic illnesses like diabetes mellitus have high rates of depressive symptoms (de Groot, Jacobson, Samson, & Welch, 1999; Renn, Steers, Jay, & Feliciano, 2013), but not necessarily higher rates of MDD or persistent depressive disorder (Fisher, Glasgow, & Strycker, 2010; Fisher, Mullan, et al., 2010).

Acute medical illnesses such as stroke (Sagen et al., 2010), Parkinson's disease (Caap-Ahlgren & Dehlin, 2001), pancreatic cancer (Jia et al., 2010; Mayr & Schmid, 2010), coronary heart disease (Kubzansky & Kawachi, 2000), and myocardial infarction (Martens, Hoen, Mittelhaeuser, de Jonge, & Denollet, 2010) are also associated with depressive symptoms. Neurological findings suggest that cerebrovascular disease (particularly ischemic small-vessel disease) may be related to the onset of late-life depression (Rapp et al., 2005). Although it is unclear whether these illnesses directly cause depression or the depression is the result of the life changes brought on by the illness, recovery from these diseases (when possible) will help alleviate depressive symptoms.

Drug and Alcohol Abuse

The next step in establishing a diagnosis is to determine to what extent the person drinks alcohol or uses drugs. Often substance abuse or dependence disorders are strongly associated with depressive symptoms (Gunnarsdottir et al., 2000; Merikangas & Avenevoli, 2000; Ostacher, 2007). Scientists have debated whether depressive symptoms are a consequence of substance abuse and the problems related to this disorder, or whether the substance use is a means of self-medicating depressive symptoms. The psychiatric and substance abuse fields are slowly moving toward the co-management of depression and substance abuse, and while abstaining from substances does often clarify the diagnostic picture, it is often very unlikely that someone who is abusing substances and has depression will be able to abstain without

treatment. Therefore, when these two conditions do present together, clinicians generally ascribe a dual diagnosis and attempt to untangle which disorder was apparent first through gathering a thorough diagnostic history.

In determining the best course of action regarding treatment, it is crucial to get a list of all medications (both prescribed and over-the-counter) the person uses, given that the side effects of many medications can cause or contribute to the depressive symptoms observed. This is particularly true with older adults, who are more vulnerable to the side effects of medication. For example, in a review of late-life depression, Dick, Gallagher-Thompson, and Thompson (1996) note that some medications, such as antihistamines, antihypertensives, some antiparkinsonian drugs, and some pain medications, commonly cause symptoms of depression. In addition, diuretics, synthetic hormones, and benzodiazepines have also been noted to contribute to depressive symptomatology (Cooper, Peters, & Andrews, 1998). The higher the number of drugs the person takes, the higher the risk for medication side effects and drug–drug interactions—a situation that emphasizes the need for good assessment of drug regimens.

GRIEF AND BEREAVEMENT

Grief over the loss of a special person or the presence of a major life stress or change can also complicate attempts to diagnose depressive disorders. Although *bereavement* may produce a grief response that mimics symptoms of depression, it was previously an exclusion for a diagnosis of MDE or a mood disorder (bereavement in the *DSM-IV-TR* was assigned a V-Code falling under Additional Conditions that may be a Focus of Clinical Attention). This exclusion was originally intended to prevent misdiagnosing "normal" grief as depression (Maj, 2008). Therefore, the removal of the bereavement exclusion has created controversies in the field; some clinicians criticized that bereavement was the only psychosocial stressor to exclude an individual from an MDE diagnosis (Wakefield et al., 2007), whereas others conceptualize grief as a normal reaction to loss and are loathe to pathologize it.

The *DSM-5* recognizes that a significant psychosocial stressor, such as a loss of a loved one, can trigger a mood disorder. Because of the overlap between "normal" grieving and depression, careful consideration is given to delineate what is a normal or appropriate response, with consideration given to the person's history and cultural norms. In making this distinction, clinicians must use their judgment to decide whether symptoms (e.g., sadness, weight loss) are appropriate for the loss or whether the symptoms more resemble those associated with a depressive episode. For example, grieving is typically classified by feelings of emptiness and loss, whereas depression is associated with a persistent sadness and an inability to experience pleasure or happiness. Also, grief is often experienced in waves of dysphoria, longing, and/or yearning, typically brought on by reminders of the deceased. These pangs of grief might also include positive emotions associated with these memories. In contrast, the unhappiness of depression is persistent and pervasive, and not associated with specific thoughts or memories.

Although it is possible that those with uncomplicated bereavement or adjustment disorder can develop a depressive disorder, little is known about the extent to which grief can develop into depression (Boelen, van de Schoot, van den Hout, de Keijser, &

van den Bout, 2010; Wellen, 2010). However, when bereavement and a depressive episode co-occur, the individual often experiences more severe functional impairment and a worse prognosis (Shear et al., 2011; Zisook, Simon, et al., 2010) than bereavement not accompanied by depression. Individuals with other vulnerabilities to depression (e.g., poor social support, trauma history, increased stressors) may be more apt to experience a major depressive episode with bereavement (Ellifritt, Nelson, & Walsh, 2003; Shear et al., 2011).

Depression Due to Other Psychiatric Disorders

Adults with other psychiatric disorders can have co-occurring depressive symptoms, and thus establishing a differential rule-out for these other disorders is often important. For instance, people with anxiety disorders, particularly generalized anxiety disorder, report feelings of sadness and hopelessness (Hopko et al., 2000). Co-occurring mood and anxiety disorders are also more commonly reported in middle-aged and older women than men (Byers et al, 2009). When under stress, people with personality disorders will also report significant symptoms of depression (Petersen et al., 2002). In fact, they can become quite acutely depressed. Specifically, depressive episodes are most prevalent with avoidant, borderline, and obsessive-compulsive personality disorders (Rossi et al., 2001). Furthermore, personality disorders have an association with a longer remission onset from a depressive episode (O'Leary & Costello, 2001). Finally, depression is common in prodromal phases of schizophrenia and is a recurrent feature in bipolar disorder.

Late-Life Depression

Depression, although not a natural consequence of aging, is one of the most common mental health disorders that older adults experience. Prevalence rates differ depending on the population surveyed and the settings observed (see Epidemiology section). Older adults present differently than younger populations in that they are less likely to report feeling sad or depressed (Fiske, Wetherall, & Gatz, 2009) or symptoms of guilt (Gallagher et al., 2010) and may report more anhedonia, memory problems (in the absence of dementia), and somatic symptoms such as fatigue, decreased appetite, and muscle pain (Kim, Shin, Yoon, & Stewart, 2002). In addition, because older adults are more likely to have chronic illnesses, the presence of physical illnesses as well as the side effects of medications taken to treat these conditions can overshadow or worsen symptoms of depression (Areán & Reynolds, 2005), which can further complicate diagnosis. In older populations, depression is also associated with increased mortality and health service usage. This association highlights the importance of early recognition, differential diagnosis, and treatment of this disabling illness.

EPIDEMIOLOGY

The patients described in this chapter are representative of a growing number of people in the United States suffering from depressive disorders. Several large-scale epidemiological studies on mental illness have taken place in the United States. The Epidemiological Catchment Area Study (ECA) was conducted in the 1980s (Regier,

1988) and was the first to definitively determine the prevalence of psychiatric problems in the United States. However, the generalizability of the ECA was limited, as data was collected at five sites. The second study, called the National Comorbidity Survey (NCS; Kessler, McGonagle, Zhao, et al., 1994), was carried out on a nationally representative sample of the United States at the time of data collection. The NCS focused specifically on English-speaking adults between the ages of 18 and 65 and was mostly concerned with the prevalence of co-occurring *DSM-III-R* psychiatric disorders in the United States.

The NCS was replicated a decade later to examine the prevalence for the *DSM-IV* and the *International Classification of Disease, version 10* (*ICD-10*) psychiatric disorders and to provide age-of-onset estimates for mental health disorders in a representative U.S. sample (NCS-R; Kessler et al., 2004; Kessler & Merikangas, 2004). The data from these studies demonstrate that the prevalence of depressive disorders varies from population to population; therefore, the following discussion will present the prevalence of depressive disorders by different populations. As the *DSM-5* was released in May 2013, no updated national prevalence data were yet available at the time of this writing.

COMMUNITY SAMPLES

Depressive disorders are serious and relatively common. Based on *DSM-IV-TR* criteria, the lifetime prevalence, or the number of persons who have ever experienced any type of mood disorder, is 20.8% (Kessler et al., 2005). The NCS-R (Kessler et al., 2005) found a lifetime prevalence for an episode of major depression to be 16.6% in a community-dwelling sample, with a 12-month prevalence of 6.6% (Kessler et al., 2003). Previous estimates of MDE were as low as 5.8% (Regier, 1988) using *DSM-III-R* diagnostic criteria. These studies also indicate that in a given 6-month period, approximately 3% to 9% of the general population will experience an episode of major depression (Kessler, McGonagle, Zhao, et al., 1994; Regier, 1988). The lifetime prevalence for dysthymic disorder is lower than the rates for MDD. According to the NCS and the NCS-R (Kilzieh, Rastam, Ward, & Maziak, 2010), between 2.5% and 6% of the general population has had a period of Persistent Depressive Disorder, pure dysthymic syndrome in their lifetimes. No nationally representative prevalence data are yet available for the new *DSM-5* diagnostic label of persistent depressive disorder.

PREVALENCE BY GENDER

The ECA and the NCS show differential prevalence by gender. In the ECA studies, lifetime prevalence of affective disorders for adult women average 6.6%, whereas in the NCS, prevalence is significantly higher at 21.3% (Kessler, McGonagle, Nelson, et al., 1994; Regier, 1988). The lifetime prevalence for men was 8.2% in the ECA and 12.7% in the NCS. Although prevalence for depression varied between these two studies, a consistent theme emerges: More women than men report having depressive episodes. The most recent nationally representative prevalence data from the NCS-R found that women are at a 1.5-fold increased risk (compared to their male counterparts) of developing a mood disorder over their lifetime, and a 1.7-fold increased risk of developing MDD specifically (Kessler et al., 2003; Kessler et al., 2005). This

difference between men and women has been found repeatedly throughout the world and thus appears to be accurate reflections of true differences in the prevalence of the disorder between men and women (Kessler, 2003). Although the reasons for these differences are relatively unknown, some speculate that sex differences in biological makeup, differences in cognitive and behavioral patterns of mood control (Nolen-Hoeksema, 2000), and social influences, including differential expectations for the two genders, account for the difference in prevalence (Kilzieh et al., 2010).

Prevalence by Age Cohort

The prevalence of depressive disorders in the United States varies by age, with the NCS-R reporting a peak in 12-month prevalence of MDD during the ages 18–29 (Kessler et al., 2003). Prevalence in this age group is threefold higher than the prevalence in individuals 60 years or older; rates drop to a 1.8-fold and 1.2-fold increased risk for adults aged 30–44 and 45–59, respectively (Kessler et al. 2003). The NCS-R included individuals over the age of 60 and up to the age of 75, which is an improvement over the demographics in the previous ECA and NCS samples (Kessler & Merikangas, 2004). As Burke, Burke, Rae, and Regier (1991) first pointed out, rates for all psychiatric disorders are increasing with each decade, indicating that disorders like depression may be influenced by cohort effects, including willingness to self-disclose symptoms and differences in measures utilized (Richards, 2011). However, the information presented by the NCS-R on the differential prevalence rates of depression between younger and older people is limited and does not include our fastest-growing segment of the population, the "oldest-old" (those age 85 and older). With the preceding caveat in mind, it is important to highlight what is known about the prevalence of depression in older adults.

The prevalence of depression among older adult populations is one of the highest of any mental disorder (Baldwin, 2000; Kessler et al., 2005). The NCS-R reports lifetime prevalence of mood disorders for individuals over the age of 60 to be 11.9%, with the majority of these cases accounted for with the diagnosis of MDD (10.6%; Kessler et al., 2005). However, it is important to keep in mind that the prevalence of depression varies substantially by population studied (e.g., NCS-R study did not include institutionalized older adults), and is affected by other sociodemographic variables such as gender, socioeconomic status, and race/ethnicity. Also, the difficulties in detecting depression in older adults (see Late-Life Depression) make this a difficult population from which to obtain precise epidemiological data.

Prevalence in Minorities

Rates of depression also vary by ethnic group. According to the NCS data, African Americans have rates of depression similar to those of the Caucasian population. Approximately 3.1% of African Americans have had an MDD episode, and 3.2% have had persistent depressive disorder, pure dysthymic syndrome (Jackson-Triche et al., 2000). However, Asian Americans have the lowest rates, with only 0.8% reporting that they had experienced an MDE and 0.8% experiencing persistent depressive disorder, pure dysthymic syndrome (Jackson-Triche et al., 2000). Hispanics/Latinos were found to have an interesting presentation of prevalence that depended on immigration

status. According to Alderete, Vega, Kolody, and Aguilar-Gaxiola (1999), Hispanics/Latinos who recently emigrated from Latin America were less likely to have depression than Hispanics/Latinos who were born and raised in the United States. Hispanics/Latinos who were U.S.-born had rates of depression much like the rates of Caucasians (3.5% for MDD and 5% for persistent depressive disorder, pure dysthymic syndrome), whereas immigrants reported only half the prevalence of U.S.-born Hispanics. Although unconfirmed empirically, Vega, Kolody, Valle, and Hough (1986) believe that lower rates in immigrants result from a heartiness factor; those who are able to withstand the stress related to immigration are more likely to cope with stress related to depression.

There are two relatively new studies aimed at capturing higher numbers of minorities in epidemiological research: First, the National Latino and Asian American Study (NLAAS), is a household survey that includes nationally represented samples of adults from various ethnic groups (i.e., eight different ethnic and subethnic groups including Latinos, Asian-Americans, African Americans, and non-Latino Whites) (Alegría et al., 2004). Second, National Survey of American Life (NSAL), a household survey of community dwelling African-American and Black adults (Caribbean). In a recent study, the data from the NLAAS, the NCS-R, and the NSAL were statistically treated and combined into a single dataset ($n = 8762$). This study found the 12-month prevalence rates of depressive disorders was higher than that found in earlier epidemiological studies; 5.4% for Asians, 10.8% for Latinos, and 8% for African-Americans compared to 11.2% for non-Latino Whites (Alegría et al., 2008). This study also confirmed that of those with depressive disorders, an alarming number did not receive any kind of mental health treatment or received inadequate treatment (Alegría et al., 2008), highlighting the need for better assessment and treatment of depression for diverse groups.

PREVALENCE IN SPECIAL SETTINGS

Prevalence of depression in certain settings is greater than what has been found in the general community. For instance, people who have depression are more likely to seek help in primary care settings (Wagner et al., 2000). Estimates vary, but most studies indicate that what used to be referred to as minor depression is the most common depressive disorder, with as many as 25% of patients meeting diagnostic criteria (Wagner et al., 2000). Although the prevalence of depressive disorders may be high, recurrence is lower in these settings than in the community. According to van Weel-Baumgarten, Schers, van den Bosch, van den Hoogen, and Zitma (2000), patients treated in primary care medicine are less likely to suffer a relapse or remission than those treated in psychiatric settings. However, psychiatry tends to manage more severely depressed patients, and thus this finding is likely an artifact of the populations served in each setting.

Another setting with high rates for depression is long-term care. Approximately 32% of people living in assisted living facilities experience MDD (Waraich et al., 2004), with new episodes occurring in 31.6% of patients within the first 12 months of admittance (Hoover et al., 2010). The causes for higher prevalence of depressive disorders in nursing home facilities may vary but most likely include loss of functional independence, loss of familiar surroundings, decreased access to pleasant activities or

loved ones, and comorbid physical illnesses. Given the impact that depressive disorders have on rehabilitation, the high rate of these disorders in these settings is cause for concern and argues for more vigilant and proactive treatment of depression in long-term care.

PSYCHOLOGICAL AND BIOLOGICAL ASSESSMENT

The assessment of depression has evolved over the decades, but many issues and controversies about the most adequate means of detecting this disorder still remain. Controversies over cultural differences, age differences, and the setting in which a client is being evaluated are still under investigation. This section focuses on the strengths and weaknesses of different methods for assessing depression, ranging from screening instruments to structured clinical interviews.

ASSESSING THE INDIVIDUAL WITH DEPRESSION

The most common way to assess for depressive disorders is by conducting in-person interviews with patients. The interviewers, usually mental health professionals or trained clinic workers, ask patients questions regarding the current episode of depression, including the symptoms patients are experiencing, how long they have been experiencing them, what they think caused the depression, and what they would like to do about the depressive episode. In addition, intake clinicians will also ask about family and personal history, past and current medical history, previous psychiatric history, and the impact of the depression on day-to-day functioning. All this information is compiled to determine whether patients have a depressive disorder, the type of disorder they have, and the degree to which they are suffering. This information is then used to determine the appropriate treatment.

Most mental health professionals use their own methods of assessment. Some will conduct an open-ended interview that is guided not by any instrumentation, but only by patients' responses to questions. Although this method is most commonly practiced, it also carries the greatest risk of misdiagnosis, particularly if the interviewer is not an expert in depressive disorders. Because of this risk, many mental health organizations prefer to use a combination of an open-ended interview with a screening instrument or a guide, such as a semistructured interview form, to help remind clinicians to ask for all relevant information. In using a screening instrument or semistructured interview, it is imperative that the instruments chosen be highly reliable and valid. Other than a medical examination to rule out physical causes for depressive symptoms, there is no biological test to diagnose depression, so accurate diagnosis rests with clinicians and the instrumentation used to confirm a diagnosis.

Screening Instruments

In many health settings, practitioners are concerned with identifying as many people as possible who have the disorder so that quick and effective interventions can take place. This tradition comes from medical practice, where physicians routinely conduct medical tests when they suspect a particular illness. These screening tests help the

doctor determine whether further tests are needed to make a specific diagnosis. For instance, when a patient sees a doctor about symptoms of fatigue, the physician will likely order blood and urine screens to determine whether the fatigue is due to anemia, diabetes, or mononucleosis. Standardized screening instruments are used for similar purposes in mental health. Screening instruments should be highly sensitive; that is, they should detect depression in everyone with the disorder. Otherwise, their utility is limited. Once someone screens positive for depression, further assessment is required to confirm a diagnosis.

The most common mechanism for diagnosing depression in adults is through self-report measures. The *DSM-5* proposed that one such measure, the Nine-Item Patient Health Questionnaire (PHQ-9; Spitzer, Williams, Kroenke, Hornyak, & McMurray, 2000; see below for more detail) be used as an "emerging measure" for future research and clinical evaluation to monitor treatment progress. However, there are numerous other self-report measures that are well-represented in the literature and clinical practice, including the Beck Depression Inventory (BDI; Beck, 1961; also, BDI-II; Beck, Steer, & Brown, 1996), the Center for Epidemiological Studies—Depression Scale (CES-D; Radloff, 1977), the Zung Depression Scale (Zung, 1972), the Montgomery Asberg Depression Rating Scale (MADRS-S; Montgomery & Asberg, 1979), and the Profile of Mood States (POMS; Plutchik, Platman, & Fieve, 1968). Because some of these measures contain items that are related to somatic symptoms (e.g., fatigue) and are frequently scored in a depressed direction by older adults who have acute physical or chronic illnesses (Street, O'Connor, & Robinson, 2007), some self-report measures have been designed specifically for detecting depression in older adults, such as the Geriatric Depression Scale (GDS; Yesavage et al., 1982). A patient completes these instruments and indicates the degree to which he or she has experienced symptoms over a specified period (e.g., 1 week, 2 weeks), and then the instrument is hand-scored by the person administering the scale. A patient's score on the instrument reflects the severity of depressive symptoms.

These instruments are considered cost-effective and efficient. They are useful in primary care settings in making quick diagnoses, especially when followed with a second-stage interview (Schmitz, Kruse, Heckrath, Alberti, & Tress, 1999). However, they are often too inclusive in that they tend to identify some people as having depressive symptoms who do not. They also differ in their assessments of depression and specifications within the diagnosis. For example, the BDI and the MADRS-S are equivalent in their assessment of depression, but the MADRS-S has a greater focus on core depressive symptoms than does the BDI (Svanborg & Asberg, 2001). Additionally, and of late, many health-care providers are using these instruments for determining a diagnosis. An issue that arises here is that these instruments are designed to be screening devices and not diagnostic tools. Furthering the problem, research indicates that such scales may be efficient in identifying psychological distress that might then be erroneously identified as major depression (Wakefield, Baer, & Schmitz, 2010).

Because of the prevalence of depression in primary care medicine, several instruments have been created specifically for use in that environment. These instruments are meant to raise a red flag to the provider so that a more thorough assessment of depression can be conducted. The Primary Care Evaluation of Mental Disorders (PRIME-MD; Spitzer et al., 1994) is a good example. The patient completes a brief

questionnaire in which two questions are red flags for depression. If the patient endorses one of the two red-flag questions, then the provider asks more specific questions to finalize the diagnosis. The PRIME-MD has satisfactory reliability and validity (Spitzer, Kroenke, & Williams, 1999). The Nine-Item Patient Health Questionnaire (PHQ-9; Spitzer, Williams, Kroenke, Hornyak, & McMurray, 2000) is a self-administered depression module adapted from the PRIME-MD. Like the PRIME-MD, it has strong internal reliability in a primary care setting (Cronbach's alpha = 0.89), excellent test-retest reliability, as well as good criterion and construct validity (Kroenke, Spitzer, & Williams, 2001). In addition, the PHQ-9 has validity in individuals of different ages and from diverse cultural backgrounds, such as Latinos, African Americans, and people of Asian descent including Thai, Korean, and Chinese, as well as individuals from Nigeria and Kenya (Adewuya et al., 2006; Diez-Quevedo, Rangil, Sanchez-Planell, Kroenke, & Spitzer, 2001; Han et al., 2008; Huang et al., 2006; Lotrakul et al., 2008; Omoro et al., 2006; Yeung et al., 2008).

Another brief self-report questionnaire for medical patients is the Beck Depression Inventory—Primary Care (BDI-PC; Beck, Guth, Steer, & Ball, 1997). This seven-item questionnaire consists of some of the same items from the full BDI and instructs the patient to rate symptoms occurring over the past 2 weeks on a 4-point scale. In research examining the BDI-PC as a screening measure for MDD, it has been shown to have high internal consistency in primary care outpatient settings (Cronbach's alpha = 0.85; Steer, Cavalieri, Leonard, & Beck, 1999) and in medical inpatients as well (Cronbach's alpha = 0.86; Beck et al., 1997; Parker, Hilton, Hadzi-Pavlovi, & Bains, 2001). When using a cut score of 4 and greater, it yielded excellent sensitivity (97%) and specificity (99%; Steer et al., 1999). Researchers noted that an advantage of the BDI-PC is that it has not been found to be correlated with age, sex, or ethnicity/racial status (Beck et al., 1997; Winter, Steer, Jones-Hicks, & Beck, 1999).

Other structured screening instruments designed for primary care include the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) and the Mini-International Neuropsychiatric Interview-Screen (MINI-Screen), a shorter version of the MINI that is available and described in more detail in the following section. The HADS is used in medical and community populations as a quick screen for anxiety and depressive symptoms in patients with physical illness. In an attempt to reduce confounds of depression diagnoses in the medically unwell population, the screen does not assess somatic symptoms. However, the trade-off is that this renders it less sensitive than other measures at screening for depression (Brennan, Worrall-Davies, McMillan, Gillbody, & House, 2010) and for detecting depression in some minority groups that tend to report more somatic symptoms than affective symptoms.

Another measure used to assess depressive symptom severity in a time-efficient manner is the Quick Inventory of Depressive Symptomatology (QIDS; Rush et al., 2003). The QIDS is a 16-item inventory developed to assess the nine *DSM-IV-TR* criterion symptom domains (i.e., sad mood, energy/fatigue, appetite and sleep dysfunction, etc.). The inventory is available in both self-report (QIDS-SR16) and clinician-rating forms (QIDS-C16), and both forms have demonstrated a high degree of internal consistency (Cronbach's alpha = 0.86 and 0.86 respectively) and acceptable psychometric properties (Trivedi et al., 2004).

Two additional screening measures for depression are the General Health Questionnaire (GHQ; Goldberg, 1972) and the World Health Organization's Well-Being

Index (WHO-5; World Health Organization [WHO], 1990). Both measures are used in community and nonpsychiatric clinical settings, such as primary care. The GHQ is a screening instrument used in primary care and general practice to detect psychiatric disorders. The original scale included 60 questions intended to capture the patient's somatic and psychiatric symptoms in less than 10 minutes. The test creators found a 0.80 correlation between clinical assessment and GHQ score (Goldberg & Blackwell, 1970). More recent modifications of the scale include 12-item, 20-item, 28-item, and 30-item questionnaires. The WHO-5 was adapted from the original 28-item questionnaire of quality of life in patients with diabetes. The five items chosen cover positive mood, vitality, and general interest. Although originally developed as a well-being index, the WHO-5 has been validated as a depression-screening tool for use with older adults (Bonsignore, Barkow, Jessen, & Heun, 2001).

STRUCTURED AND SEMISTRUCTURED CLINICAL INTERVIEWS

Once a person screens positive for a depressive disorder, the next step is to confirm the diagnosis, which is best done by using a structured or semistructured interview. As stated earlier, most people who are expert in the diagnosis of depression disorders do not need the assistance of a structured instrument. However, because experts are not always available and employing them can be quite costly, structured and semi-structured interviews have been developed for use by less-experienced personnel or for use in research or facility protocols to increase consistency in assessment. To address the concerns of managed-care systems, these interviews have utility in that they increase standardization in service delivery, increase consistency in diagnosis, and allow for tracking outcomes (Rogers, 2001). The best-known instruments are the Structured Clinical Interview for *DSM-IV* and the Composite International Diagnostic Interview. Another short structured diagnostic interview is the Mini-International Neuropsychiatric Interview. The Diagnostic Interview for *DSM* (DIS) has also been used widely but has been largely replaced by the CIDI and so will not be discussed in this chapter.

The Structured Clinical Interview for DSM-IV The Structured Clinical Interview for *DSM-IV* (SCID; First, Spitzer, Gibbon, & Williams, 2002) was developed for clinical research to determine the presence of *DSM-IV* disorders. It is a semistructured interview to be used by formally trained staff. Although interviewers use the instrument as a guide to structure the interview, the interviewer can also rely on his or her judgment in interpreting a patient's answers to questions. Because there is a reliance on clinical judgment, the SCID functions best when administered by a trained mental health professional.

The SCID interview is divided into three sections: (1) a historical overview of the presenting complaint; (2) a screening list to determine beforehand whether the patient has symptoms of MDD, alcohol or substance abuse, obsessive-compulsive disorder, and anxiety disorders; and (3) the different diagnostic modules to reflect all the Axis I diagnoses of *DSM-IV*. Although the SCID has been used extensively in research studies, it has only fair validity and reliability. According to the SCID's creators, this instrument has a kappa coefficient of agreement equal to only 0.31 in nonpatient samples, indicating poor validity.

The utility of the SCID compared to physician diagnoses of depression has been demonstrated (Sanchez-Villegas et al., 2008). The main advantage to the SCID is its structured nature, which decreases the amount of variation of diagnosis from clinician to clinician. However, it is still a costly instrument in that staff administering the SCID must be trained in its use and must be of a professional level. However, costs can be lowered while maintaining the effectiveness of the assessment by the use of trained research assistants rather than senior investigators to administer the test (Miller et al., 1999).

Composite International Diagnostic Interview The Composite International Diagnostic Interview (CIDI) was developed by WHO for the purpose of providing a variety of diagnoses that are in accord with definitions from the *DSM-IV*. This structured clinical interview is a fully computerized interview and so is able to attain a complexity and depth of diagnosis with carefully programmed skip patterns and flowcharts. Its great advantage is that it does not require a mental health professional to administer the instrument—in fact, the CIDI can be used as a patient-only-administered instrument, although it is also common for a researcher to administer it. Because the program makes the diagnosis, the researcher giving the interview does not need to make any independent clinical judgments (Kessler & Üstün, 2004).

The obvious benefits of the CIDI are that it is computerized and thus cuts down on costs of training interviewers and of using health practitioners to make diagnoses. There are, however, some drawbacks to the use of the CIDI. One important one is that because it is computerized, certain disorders may be more difficult to diagnose because of individuals' desire to maintain secrecy or denial of mental disorders (Thornton, Russell, & Hudson, 1998). Additionally, because it is computerized, differences among individuals that the program does not account for cannot be adjusted within the interview. However, the CIDI can be a useful tool provided that it is used with a follow-up interview with a clinician.

The Mini-International Neuropsychiatric Interview The Mini-International Neuropsychiatric Interview (MINI) was developed by Sheehan and colleagues (1998) to assess the most common *DSM-IV* and *ICD-10* psychiatric disorders. With a 15-minute administration time, the MINI is purported to be shorter than the typical interviews used in research settings but is more thorough than screening tests. Like the CIDI, the MINI is advantageous in that it does not require a mental health professional to administer the instrument, thus saving costs and freeing time for mental health professionals to focus on other critical issues. The interview items focus on current symptoms (except for bipolar disorder) that are most routinely asked about by clinicians. This allows for a shorter administration time than other interviews, such as the SCID, that probe for past symptomatology as well.

Research testing the validity of the clinician-rated MINI has shown good to very good concordance with other clinician-rated diagnostic interviews (SCID and the CIDI), and it has excellent interrater reliability (kappa > 0.79) for all diagnostic categories and good test-retest reliability (kappa > 0.63) for all diagnostic categories except simple phobia and current mania. The MINI also demonstrated very good specificity (> 0.86 with SCID; > 0.72 with CIDI) and very good positive and negative predictive values for most diagnostic categories. For more details, see Sheehan et al., 1998.

The MINI is also available in other formats, including a longer version for the academic researcher called the MINI-Plus that includes 23 psychiatric disorders (as opposed to 19); a patient-rated version for use in outpatient settings (the MINI-PR); a version for children and adolescents (the MINI-Kid); and a shorter screening instrument, the MINI-Screen (as previously discussed), for primary care. There are also multiple translated-language versions and a computerized version now available whose properties are currently being investigated.

COMMENT

Determining the presence of a depressive disorder requires skill and effort in gathering information about the depression and its potential causes. The most efficient method to determine the presence of a depressive disorder is to first screen the patient and then, if the screening is positive, to perform an in-depth interview.

ETIOLOGICAL CONSIDERATIONS

The most debated topic in depression research is etiology. To date the majority of research in this area has focused on MDD, with very little research on dysthymic disorder. Other specified or unspecified depressive disorder appears to be related to whatever is thought to be the comorbid cause. Most scientists now believe that depressive disorders are multifaceted, with causes resulting from the interactions of psychological, social, and biological factors (Kendler, Thornton, & Prescott, 2001; O'Keane, 2000). For example, stressful life events have been found to increase the risk for developing depression (Kendler & Gardner, 2010; McIntosh, Gillanders, & Rodgers, 2010). However, the person's coping style, social support, and genetic makeup all mediate the impact that stress has on depression (Fountoulakis, Iacovides, Kaprinis, & Kaprinis, 2006; Vergne & Nemeroff, 2006). A person who loses his job but has good social support and coping skills will be less likely to develop depression than another unemployed person who has limited coping skills and no social support. Though depression is related to many variables, their intermingling can most clearly predict the development of depression, rather than any single factor determining the onset. Genetics, learning, and life experiences all work together to cause depression.

FAMILIAL AND GENETIC

The most fascinating research on the etiology of depression has been the recent work on the role of genetics in mental health. With the mapping of the human genome, the prospect of clearly identifying the influence of genetics on mental health is within reach. However, with depressive disorders, the contribution of genetics may take longer to uncover than for other disorders that have already demonstrated a clear genetic and biological cause (i.e., schizophrenia). Although past evidence from twin studies has been able to demonstrate some genetic involvement in depressive disorders, those links have thus far been weak.

Historically, the principal method for studying the influence of genetics on psychopathology was to compare the concordance of depression in identical twins (MZ; monozygotic twins), who originate from the same gene and are effectively

genetically identical individuals, to that of fraternal twins (DZ; dizygotic), who share only half of their genes and thus are genetically similar to siblings. Because the frequency of twin births is low, genetic researchers also observe the rates of depressive disorder in first-degree relatives (often parents and children). According to the twin studies, MZ twins have greater concordance rates for depressive disorders than do DZ twins (Englund & Klein, 1990). More recent work by Kendler and Prescott (1999) evaluated MDD in DZ and MZ twins according to sex, and estimates the odds ratios for a lifetime diagnosis of MDD to be equal to 39% and is approximately the same for male and female twins. Family studies also find that the onset of depression is more likely in people with relatives with depression than in those who do not have family members with depression (Byers et al., 2009). The rates are not that compelling, however, with relatives having only a 21% risk for developing depression (Kupfer, Frank, Carpenter, & Neiswanger, 1989). Overall, the aggregate estimated rate of heritability for depression is between 31% and 42% (Sullivan, Neale, & Kendler, 2000).

However, recent research in MZ and DZ twins suggests that there is higher heritability for all unipolar depressive disorders combined compared to MDD alone. Additionally, recurrent early-onset MDD seems to be the most heritable form of the unipolar depressive disorders, with research estimating that approximately half of first-degree relatives and one-quarter of extended relatives of individuals with recurrent, early-onset MDD suffer from at least one mood disorder (Zubenko, Zubenko, Spiker, Giles, & Kaplan, 2001). Rates of heritability for MDD, when correlated with other unipolar depressive disorders (e.g., atypical depression, dysthymic disorder, and adjustment disorder with depressive features), were moderately higher than heritability of MDD alone. These findings suggest that some depressive disorders (e.g., MDD, persistent depressive disorder, pure dysthymic syndrome) may be reflections of the same underlying genetic liability (Edvardsen et al., 2009).

Direct genetic comparisons are becoming a more popular method for determining genetic links to mood. These methods are considered superior to the methods discussed previously, because DNA is a specific measure that is unlikely to be modified by environmental influences. The results from twin and family studies cannot account for the impact of learning on development of depression, whereas DNA is less likely to be influenced by personal experience. Additionally, molecular genetic analysis allows for specific genetic hypotheses to be tested. DNA studies are able to compare depressed with nondepressed controls on characteristics of certain genes that are associated with neurotransmitters related to depressive disorders. Although still in its infancy, this research has been very helpful in confirming the role of genetics in the development of depressive disorders. For instance, Dikeos and colleagues (1999) studied whether the genetic location of the D3 dopamine receptor differed in patients with MDD as compared to those with no history or current MDD. The investigators observed that genotypes carrying the allele (DNA structure) associated with D3 polymorphisms were found in 75% of the MDD patients and in 50% of the controls, suggesting genetic influences in MDD. Other studies, however, have not found such robust effects (Frisch et al., 1999; Neiswanger et al., 1998; Qian et al., 1999). More recently, Green and associates (2010) demonstrated an increased risk for recurrent MDD in individuals who have a variation in a gene that provides instructions to cells for making calcium channels. These channels are an important feature of cells, as they are involved in intercellular communication and generating and

transmitting electrical signals, although their exact role in brain tissue is still unclear (Splawski et al., 2004). At best, the literature on the genetics of depressive disorders suggests a propensity to develop these disorders but that this propensity can be offset by learning and environmental influences.

NEUROANATOMY AND NEUROBIOLOGY

Over the past 5 years, there has been considerable advancement in our understanding of the neuroanatomy and biology of depression. In the quest to uncover biological markers of mental disorders, much research effort has gone into determining biological determinants of depression, with a specific focus on the brain structures that appear to be associated with depression, neurocircuitry, and neurotransmitters. However, to date no laboratory test has been uncovered as a valid diagnostic tool for depressive disorders.

Neuroanatomy and Neurocircuitry Research into brain regions associated with depression is ongoing, but current brain theories of depression argue that several brain systems interact to regulate mood in response to stress. Research data from functional neuroimaging (fMRI) studies, research on people with brain damage, and positron emission tomography (PET) suggest that four brain regions are associated with depression. The first is the *amygdala*, which is responsible for memory of emotional reactions to stimuli. This part of the brain interprets the emotional salience of stimuli, and when there is a threatening stimulus, it produces an emotional reaction that triggers the brain into action. Next is the *orbitofrontal cortex*, which is responsible for cognitive processing and decision making. This part of the brain is in part responsible for putting logical meaning to the stimulus and for determining what should be done about the stimulus. The *dorsolateral prefrontal cortex* is responsible for affect regulation, planning, decision making, intentionality, and social judgment. Finally, the *anterior cingulate cortex* is also involved with depression and is responsible for error detection, anticipation of tasks, motivation, and modulation of emotional responses (Koenigs & Grafman, 2009).

These systems work together to help us navigate our environment, and when they work well and in concert, we are able to manage most problems that come our way. When we are faced with a problem to solve, whether it is social, financial, or environmental, these systems work together to first let us know there is a problem in the environment, to assess the degree of threat the problem presents with, to modulate our emotions in reaction to the problem, to decide among a series of potential solutions to solve the problem, and then to initiate behavior to either cope with or solve the problem. When any of these systems is not working properly, whether due to brain damage, congenital anomalies, or learned behavioral patterns, our chances for developing depression are increased. For instance, if the mood regulation systems in the dorsolateral cortex are not working properly, they fail to regulate the emotional reaction to the problem. This failure prevents the orbitofrontal cortex from being able to create an action plan to solve the problem. What results is the tendency to avoid, rather than solve, the problem or to overreact to the problem.

Several functional imaging studies are beginning to support the role these systems play in depression, but the work is still very preliminary. Additionally, because

depression is a rather heterogeneous disorder (people with the same diagnosis, even history, can have a very different clinical presentation), scientists are often coming up with different explanations for how these systems work, even about which systems are most important. This is partly because the expense of conducting this research is so high, and therefore the number of research participants in these studies tends to be quite small; given the heterogeneity of the illness, it is no surprise that under-sampled studies would yield heterogeneous results. Finally, although technologies such as fMRI have revolutionized the field, many scientists are now claiming that results from these experiments should be viewed with caution (Logothetis, 2008).

Neurochemistry and Transmitters Clinicians initially believed that depression was caused in part by lack of the two neurotransmitters *norepinephrine* and *serotonin*. Now, however, it is known that the dysregulation rather than the deficiency of these neurotransmitters causes depression (Moore & Bona, 2001). Antidepressants to regulate the production and distribution of norepinephrine and serotonin are effective in their ability to increase the availability of receptor sites rather than increase the production of the neurotransmitters (Veenstra-VanderWeele, Anderson, & Cook, 2000). Neurotransmitters provide an important but still only partial picture of the biological origin of depression, because abnormalities in neurotransmitter regulation do not necessarily lead to a depressed mood.

Neuroendocrinology also adds to a more complete understanding of the biological causes of depression. The most heavily researched of this area has been the link between the *hypothalamic-pituitary-adrenal (HPA) axis* functioning and adult depression over the past 40 years (Lopez-Duran, Kovacs, & George, 2009). The HPA axis is a major part of the neuroendocrine system that regulates bodily processes, including the stress response; not surprisingly, abnormal HPA axis functioning has been implicated in numerous psychiatric disorders, most notably major depressive disorder (Pariante & Lightman, 2008). Specifically, evidence points to an overabundance of *cortisol* in the systems of patients with depression. Additionally, abnormalities in thyroid functions are often related to symptoms of depression, further indicating an important role for the neuroendocrine system in depression. In a study by Ghaziuddin and colleagues (2000), neuroendocrine imbalances in adolescents with MDD as compared to their nondepressed counterparts demonstrated that depression is associated with abnormal baseline levels of prolactin as well as sharper prolactin and cortisol responses to serotonergic challenges. Evidence for such abnormalities not only yields a more complete understanding of causation but also aids in the development of more effective drug treatments.

Learning and Modeling

There is a tremendous amount of research investigating and supporting behavioral, social, and environmental influences in the development of depression. A review of this literature suggests that depressive disorders appear to be related to three psychological variables and the individual's learning history (life experiences):

1. People's cognitive appraisals of themselves, their lives, and others (Alloy et al., 2000; Beck, Rush, Shaw, & Emery, 1979).

2. Whether people proactively solve problems or avoid them (D'Zurilla & Nezu, 1999).
3. The degree to which proactive attempts to cope with stress have been successful (Folkman & Lazarus, 1988).
4. An individual's learning history could lead to the development of depressive symptoms or serve to maintain depression/dysphoria.

In this paradigm, people who have negative expectations about their ability to cope with problems generally acquire these expectations through past learning experience. Repeated failed attempts to solve problems (learning history), for instance, leave a person feeling hopeless and helpless, abandoning his or her usual methods for solving problems, and becoming depressed (Seligman, Weiss, Weinraub, & Schulman, 1980). These factors—cognitive attributions, coping skills, and learned helplessness—have all been found to be predictive of depression.

People with negative expectations or cognitive vulnerabilities are more likely to develop depression when faced with a stressor than are people who do not possess cognitive vulnerabilities. Grazioli and Terry (2000) found that in women with postpartum depression, both general and maternal-specific dysfunctional attitudes were associated with self-reported depression, particularly in women who had children who were found to be temperamentally difficult. Another study found that individuals with negative cognitive styles had higher lifetime prevalence of depression than people who were not cognitively vulnerable (Alloy et al., 2000). Therefore, people with negative perceptions of themselves and their environment are at risk for becoming depressed.

Coping skills have also been found to be related to depression. Most research has found that people who use active forms of coping, such as problem solving, are less likely to develop depression than are people who use passive forms of coping, such as avoidance. In fact, in one study, people who used an avoidant coping style were more likely to develop depression when faced with psychosocial stressors (Welch & Austin, 2001). Rumination, a repetitive pattern of thoughts and behaviors focused on one's depressed state, can also result in less effective problem solving (Donaldson & Lam, 2004). Although coping skills deficits and cognitive style contribute to depression, the interaction of these two factors seems to have the biggest impact on the development of depression. Several studies have supported this interaction in *learned helplessness*.

Originally, these theories were tested in animal models, where unsolvable problems were presented to animals and all attempts to solve the problem were met with unpleasant consequences, such as an electric shock. After repeated attempts to solve the problem failed, these animals would exhibit depressogenic behavior—withdrawal, acting as if they were in pain—and, even after a solution was presented to them, the animals would refuse to try the solution (Altenor, Volpicelli, & Seligman, 1979). Scientists have been able to draw a relationship between learned helplessness and depression in research with people. For instance, Swendsen (1997) found that people with high-risk attributional styles were more likely to experience depressed mood after exposure to negative stressful events.

A person's learning history may also play a role in the development of depression. Since the 1970s there has been a tremendous amount of interest in investigating the role that learning principles play in the development of depression. Ferster (1973)

postulated that individuals with depression did not engage in enough activities and may even avoid activities, thus leading to insufficient reinforcement for those activities. This limited engagement in activities also results in fewer opportunities to learn through experiencing those activities (contingencies of reinforcement). Lewinsohn (1974) expanded upon this theory, emphasizing depression as being the result of low levels of reinforcement contingent upon behavior. This lack of reinforcement that a person would obtain from doing something proactive would lead to less engagement in those types of behaviors in the future, eventually leading to withdrawal and isolation. According to this model, depression results from either a decrease in pleasant events or an increase in unpleasant events and speaks to the importance of considering context in the development of depression (Jacobson, Martell, & Dimidjian, 2001).

Jacobson and colleagues developed the behavioral activation model (which grew from these theories and further developed them), emphasizing that when life is less rewarding or stressful, people sometimes pull away from the world around them and find that basic routines in their life become disrupted. This disruption in routines can increase depressive symptoms and make it difficult to solve life problems effectively. In turn, this can lead to secondary problems (e.g., relationships, occupational difficulties), which maintain or further exacerbate depression. Support for these models is strong and can be found in the depression treatment literature.

Life Events

The literature is replete with data indicating that stressful life events contribute to the development of a depressive episode. Although not everyone who faces difficult problems develops depression, it is evident that prolonged exposure to psychosocial stress can precipitate a depressive episode (Hammen, Kim, Eberhart, & Brennan, 2009). Several studies have found that most depressive episodes are preceded by a severe life event or difficulty in the 6 months before onset of the episode (Kendler & Gardner, 2010). Kapci and Cramer (2000) also found that people were more likely to develop depression when they were exposed to numerous negative life events, but only if their belief in their ability to solve problems was impaired. Thus, the interaction of negative life events, coping skills, and attributions about coping skills influences whether a person will experience depression. In addition, patients with more long-term or chronic depression were more likely to report past abuse, although the causal relationship is unclear (Keitner et al., 1997).

Because depression is a multifaceted disorder, it is difficult to pinpoint the specific role life events have on the development of a depressive disorder. Most people will have to face severe life stress at some point in their lives, yet not everyone develops depression. How an individual views severe life events and the perceived control he or she feels over the situation both play an important role in determining one's vulnerability to depression. For instance, several studies find that the relationship of life events to depression is mediated by other factors such as social support, cognitive style, and coping abilities (Alloy et al., 2000; Cacioppo, Hughes, Waite, Hawkley, & Thisted, 2006). Severe life events are significantly more likely to provoke a major depressive episode in individuals without social support (Leskelä et al., 2006). Support systems give an individual external support when internal coping skills are

put to the test. Without the external support, however, an individual must rely exclusively on his or her own internal resources, which under severe duress might not be entirely effective. Therefore, although negative life events do influence the occurrence of depressive disorders, the social and psychological resources available to the person facing the stressful life event generally mediate the impact on mood.

GENDER, RACE, AND ETHNICITY

Many researchers have been trying to determine the reasons for the discrepant rates of depressive disorders across gender and racial-ethnic lines. Are the reasons genetic or biological? Is it that these populations are exposed to more stress and have fewer resources to cope with stress and therefore are more vulnerable than men and nonminority groups? Or is depression presented differently across these groups, and therefore the estimates in the prevalence for depressive disorders in these populations are inaccurate? Mental health researchers are still struggling with these questions and have only been able to give a partial explanation of why the discrepancy exists.

Some theorists believe that the reason minorities have differing rates of depressive disorder is that they present their symptoms of depression differently than do Caucasians (Escalante, del Rincon, & Mulrow, 2000; Ryder et al., 2008). Many researchers have spent years trying to discern the most appropriate way to assess depression in different cultures. Although research from the WHO indicates that depression is similar across cultures, how people from one culture report the symptoms and their cultural attitude about mental health (and its treatment) can cloud diagnoses. Screening instruments and scales that were developed for Caucasian populations can be problematic if they are simply translated without regard for translation bias. Additionally, many studies have found that the factor structures and reliabilities of these instruments tend to differ across ethnic groups, indicating that groups vary in their reports of depressive symptoms (Azocar, Areán, Miranda, & Muñoz, 2001). For instance, lower rates of depression in Asians may be attributable to their tendency to underreport affective symptoms of depression and to rely more on somatic presentation (Ryder et al., 2008).

Others have hypothesized that the different rates of depression in ethnic groups are associated with the fact that in this country, minority groups such as African Americans and Hispanics are more likely to be impoverished and to have to cope with financial and urban stress (Alexopoulos, 2005). Studies have demonstrated that socioeconomic status and exposure to trauma related to racism, urban living, and financial strain are correlated with depression and other mental illnesses such as anxiety and substance abuse (Caron & Liu, 2010; Gottlieb, Waitzkin, & Miranda, 2011; Kiima & Jenkins, 2010; Rhodes et al., 2010). Other studies have found that the rates for depression in middle class and affluent minorities are more similar to the national rates of depression as compared to middle-class and affluent Caucasians. These studies seem to argue that in the case of minority populations, increased exposure to stress is the reason for the differing rates of depressive disorder (Olfson et al., 2000).

The differing rate of depressive disorders between men and women is an interesting yet complicated finding. Researchers initially thought that the different prevalence rates resulted from reluctance on the part of men to admit feelings of depression, as

well as men's tendency to cope with stress through substance use (Shorey et al., 2011). Others suggest that the increased prevalence of depression in women is because women tend to be victims of sexual abuse and therefore suffer a significant psychosocial stressor that is not as common in men (Gaudiano & Zimmerman, 2010; Ghassemi, Sadeghi, Asadollahi, Yousefy, & Mallik, 2010; Plaza et al., 2010). Still others suggest that the willingness of women over men to seek treatment services might account for the difference in prevalence (Fikretoglu, Liu, Pedlar, & Brunet, 2010). However, because the discrepancy between men and women seems to be universal, others claim that hormonal and biological differences account for the differential prevalence rates. Whatever the differential effect, the fact remains that depression is more commonly reported in women than in men, and this issue still needs to be resolved.

COURSE AND PROGNOSIS

Research has begun to identify variables that can predict toward better or worse course and outcome, but a great deal of uncertainty still exists. Here we present the descriptive data regarding length, severity, and prognosis of depressive disorders.

Course

Beyond the basic diagnostic criteria, MDD has several delineating features. Early-onset depression tends to appear before age 20 and has a more malignant course than late-onset depression (Devanand et al., 2004; Papakostas, Crawford, Scalia, & Fava, 2007). It is also associated with a family history of depression and other mood disorders (Bergemann & Boles, 2010; Wermter et al., 2010). Late-onset depression tends to emerge in the mid-30s and is associated with fewer recurrent episodes, comorbid personality disorders, and substance abuse disorders relative to early-onset depression (Chui, Cheung, & Lam, 2011). However, there is a much greater variation in the age of onset with depression than in disorders such as schizophrenia. Second, the course of MDD tends to be time limited. The average episode lasts 6 months, although this varies greatly from person to person (Rhebergen et al., 2010). Third, MDD tends to be a recurrent disorder. Patients who have one major depressive episode have a 36.7% chance of experiencing a second; those who have two previous episodes have a 48% chance of developing a third episode. With each additional episode, chances for another additional episode increase by approximately 15% (Seemuller et al., 2010).

Persistent depressive disorder is a more chronic, long-lasting illness. The mean duration of dysthymic disorder is 30 years, and given that the symptom presentation for persistent depressive disorder has not changed much, it is thought that this statistic still holds for the newer persistent depressive disorder category. Almost half of those patients who were previously classified as dysthymic disorder will develop a major depressive episode in their lifetimes (Rhebergen et al., 2010). Those with persistent depressive disorder (pure dysthymic syndrome) have been found to have worse clinical prognosis than people with either MDD or depressive disorder, NOS (now classified as other specified or unspecified depressive disorder) and are as disabled as those with MDD (Griffiths, Ravindran, Merali, & Anisman, 2000).

Thankfully, persistent depressive disorder (pure dysthymic syndrome) is responsive to both psychotherapy and medication treatment, at least in the short term, with some studies suggesting that the most robust intervention is a combination of psychotherapy and medication (Barrett et al., 2001). Unfortunately, few people with persistent depressive disorder ever receive treatment. Fewer than half will ever receive any kind of mental health treatment unless they have also experienced a major depressive episode (Rhebergen et al., 2010).

PROGNOSIS

Early diagnosis and treatment with therapy, medication, or both result in a better chance of recovery from MDD, persistent depressive disorder, pure dysthymic syndrome, and other specified or unspecified depressive disorder (depression NOS) (Rhebergen et al., 2010). The ease of recovery from depression, however, is related to several factors. Prognosis is best when the patient is facing few stressful life events (Sherrington, Hawton, Fagg, Andrew, & Smith, 2001) and has a solid support network on which to rely (Rubenstein et al., 2007). Furthermore, individuals with an initial early recovery are less likely to develop recurring symptoms. Early improvements indicate that the patient has access to coping mechanisms that allow for a quick recovery, and this often suggests an overall positive long-term prognosis. The prognosis for persistent depressive disorder, pure dysthymic syndrome is less certain. For example, Ciechanowski and colleagues (2004) demonstrated a 50% reduction at the end of a 12-month period in depressive symptoms and functional improvement using problem-solving therapy in home-based intervention for older adults with medical illnesses, minor depression, and persistent depressive disorder, pure dysthymic syndrome. However, Klein and colleagues (Klein, Shankman, & Rose, 2006) found that adults with persistent depressive disorder, pure dysthymic syndrome improved at a much slower rate and were more symptomatic at a 10-year follow-up than were individuals with MDD. As of this writing, few treatment studies have demonstrated any long-lasting positive effect for any intervention for persistent depressive disorder, pure dysthymic syndrome.

Another factor involved in the prognosis for both MDD and persistent depressive disorder are levels of self-esteem. A higher self-esteem predicts an increasingly positive prognosis (Sherrington et al., 2001). Poor self-esteem, on the other hand, predicts a longer and more delayed recovery. The prognosis of depressive disorders is poor when they have an early onset, a premorbid personality disorder exists, and there has been a previous episode (Ryder, Quilty, Vachon, & Bagby, 2010). More intensive and extended treatment can improve the remission and maintenance of remission from MDD episodes, even with high severity of the depression, although the evidence on persistent depressive disorder is limited.

CASE STUDIES

MAJOR DEPRESSION

Case Identification R. J. was a single, 32-year-old African American woman who self-referred to mental health services for what she called "depression."

Presenting Complaints Before seeking services, R. J. had contemplated getting gastric bypass surgery and was extremely unhappy with her employment. She was managing several large projects for the company she worked for and felt that she was the only member of her staff who was doing any work. She felt that she was not trusted to do her job, was not respected for the work she did, and was being taken for granted. She was also concerned about getting the surgery, because she would need recovery time and would be unable to care for her family members. Her symptoms included feeling depressed nearly all day, every day, for the past 12 months; feeling a lack of interest in her usual activities (in this case walking and attending a weight-loss program); and increased irritability. For the past 12 months, she reported insomnia, increased appetite, and feelings of worthlessness and hopelessness about the future. She reported feelings of guilt, believed that she was being punished, and constantly worried that she was not doing enough for her family. In addition, she reported having difficulty concentrating and making decisions. Although she had occasionally felt that she would be better off dead, she was not suicidal. She did not feel that suicide was an option and had no plan to harm herself.

History R. J. was the younger of two female siblings from the northwestern section of the United States. As a child, she did not have time for friends, because she was often caring for her sick mother. She was a good student but had dropped out of high school to care for her mother. Her father had left her mother and moved out of state shortly before her mother became ill. R. J. had a large extended family but acutely felt the loss of a father figure. Her uncle had problems with drugs and was incarcerated. Subsequently, she had taken on the care of her younger niece and nephews. As an adult, R. J. had success in school (she was able to achieve her GED and was successfully taking college courses) and in her work. She believed that she had suffered from depression twice before in her adult life but had always been able to overcome the depression on her own. However, she had often turned to food for comfort and was suffering from obesity. She explained that she had never sought help for her depression before because she was busy caring for her family and did not take time for herself. Furthermore, she indicated that it was not like her to talk with someone about her feelings. She believed her mother was depressed following the loss of her husband and subsequent medical problems but was unsure of these facts, because these issues were never discussed.

Assessment R. J. presents with several interesting issues related to depression. First, she reports having no less than nine symptoms of depression, six for more than a year; she also reports having these symptoms nearly every day and that they are impairing her ability to function at work and socially. R. J. also indicates having had two previous depressive episodes that spontaneously remitted, and that her mother may have suffered from depression as well. Based on this assessment, R. J. met criteria for recurrent major depressive disorder and may have an endogenous form of the disorder.

Persistent Depressive Disorder, With Pure Dysthymic Syndrome

Case Identification B.G. was a retired, 55-year-old Caucasian man who sought services for depression after a doctor recommended he talk to a mental health professional.

Presenting Complaints B.G. stated that for the past 3 years, he occasionally felt worthless, depressed, and irritable. He reported that some days he often found it difficult to get himself going to complete his chores for the day but would somehow manage to do so. He indicated that he was unsure of whether he needed treatment, because he had "good days," but upon further probing he reported that these days were infrequent (no more than 1 or 2 days per week). Although he said he and his wife did not have marital problems, he felt guilty that she worked and he did not. The primary symptoms he complained about were occasional sadness, lack of energy, irritability, feelings of worthlessness, and guilt.

History B. G. was the oldest of five children in his family and was currently married with three children, all of whom were grown and living in other parts of the country. He completed high school and trade school afterward. He had been employed with one construction company his entire adult life. He was living with his wife at the time of his intake. He had no serious health problems other than chronic pain resulting from a back injury. B.G. retired because the back injury prevented him from performing his job. Three years ago, his wife took on a part-time job to make extra money, and B. G. began looking after the house. Prior to this visit, he had never sought mental health services, nor had he ever felt depressed.

Assessment B. G. presents with some classic symptoms of dysthymic disorder, now subsumed under the category in *DSM-5* of persistent depressive disorder; he reports having depressed mood for more days than not for more than the required 2-year period. He denied a history of manic episodes and did not meet criteria for an MDE during this 2-year period. He also met the two or more additional symptom requirements, which included such symptoms as lack of energy and low self-esteem. Although B. G. did report brief periods in which he felt "good," these symptom-free periods only occurred on average 1 to 2 days per week, and, therefore, he met the additional specification of not having been symptom free for more than 2 months at a time during the current episode. Based on our assessment, B. G. met criteria for a diagnosis of persistent depressive disorder, with pure dysthymic syndrome, late onset.

UNSPECIFIED DEPRESSIVE DISORDER

Case Identification T. J. was a 40-year-old woman who was referred by her physician for treatment of depression. According to the physician, T. J. was struggling with placing her elderly mother in a nursing home, and this struggle made her quite depressed. The provider indicated that T. J. had a recent diagnosis of hyperthyroidism and was being treated with medication.

Presenting Complaints T. J. stated that she had been feeling depressed for several months, ever since her mother had become more seriously ill and T. J. began trying to find a nursing home for her. Her primary complaints were depression and sadness nearly all day, every day; feeling slowed down; and trouble with concentration. She also indicated that having had a recent diagnosis of hyperthyroidism complicated matters for her and that she had been unable to take her medication regularly.

History T. J. was an only child who was living with her mother at the time of referral. She had a college education and had been employed as an administrative assistant for 10 years. She was divorced with no children. T. J. indicated that she had been her mother's caregiver for most of her life and that they had a "love-hate" relationship. Her mother was being verbally abusive to T. J. regarding the placement, making T. J. feel guilty. T. J. indicated that she would normally be able to let her mother's abuse roll off her back, having long ago accepted that her mother was a difficult person. However, the last 4 months were hard to cope with, even though she had a good caseworker helping her, and her mother would be placed in a pleasant assisted-living facility within the next month.

Assessment/Treatment After consideration of her symptoms, T. J.'s symptoms did not appear to meet full criteria for MDD, but it was clear to the therapist that a depressive disorder was present. What was unclear was whether the depression was primary, whether her medical symptoms were the cause of the depression, or if the client's depressive symptoms were related to a psychosocial stressor, thus a diagnosis of unspecified depressive disorder was assigned.

T. J. was encouraged to start taking her medication for hyperthyroidism and was educated about the link between the illness and depressive symptoms. T. J. and her therapist agreed to meet again in 2 weeks. At that meeting, T. J. reported that her mother had been placed in the assisted-living facility and that while she felt guilty for a few days, she found that her mother was actually quite happy at the facility. She also reported taking the medication regularly and stated she already felt much better ("like my old self"), although she was still somewhat symptomatic of depression (occasional sadness and poor energy). Now that her mother had been successfully placed, T. J. indicated that she would like to work on rebuilding her social life.

SUMMARY

Depressive disorders are common and widely studied. Given the extent of our knowledge of MDD and what was previously classified as dysthymic disorder, research continues to address the best means of recognizing depression, how to treat depression in different settings and in different cultures, and further clarification of the etiology of these disorders. The causes and symptoms of depressive disorders are extremely variable and intermingled. The causes include both physiological and environmental factors, and the expressions of depression vary from short, severe episodes to chronic symptomatology. Because of the immense complexity of the depressive disorders, further research will aid in the ability to tailor diagnosis and therapy to each particular manifestation, to better address these disorders with medical comorbidities, and explore cross-cultural concerns in assessment and treatment.

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CHAPTER 8

Anxiety Disorders

DAVID P. VALENTINER, THOMAS A. FERGUS, EVELYN BEHAR,
and DANIEL J. CONYBEARE

MUCH OF WHAT we know about panic disorder, agoraphobia, generalized anxiety disorder, social anxiety disorder, and specific phobias is based on studies using diagnostic criteria that predate the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (*DSM-5*; American Psychiatric Association [APA], 2013). Definitions of these disorders have generally shown small changes over recent editions of the *DSM*, allowing for reasonable inferences about disorders, as currently defined, to be drawn using past studies. With this caveat in mind, these disorders are prevalent and often quite debilitating.

Anxiety disorders are commonly diagnosed in the United States, with almost one-third of individuals meeting criteria for at least one anxiety disorder at some time in their lives—a prevalence rate second only to substance use disorders (Aalto-Setälä, Marttunen, Tuulio-Henriksson, & Lönnqvist, 2001; Beekman et al., 1998; Kessler et al., 1994). In addition, these disorders lead to poor educational outcomes (Kessler, Foster, Saunders, & Stang, 1995). Goisman et al. (1994) found that about 50% of patients with panic disorder and/or agoraphobia were receiving unemployment, disability, welfare, social security payments, or some other form of financial assistance. Generalized anxiety disorder is also associated with significant costs to society due to decreased work productivity and increased use of services, particularly primary health care (Wittchen, 2002). Social anxiety disorder is associated with compromised functioning in school and at work (Liebowitz, Gorman, Fyer, & Klein, 1985; Turner, Beidel, Dancu, & Keys, 1986; Van Ameringen, Mancini, & Streiner, 1993; Wittchen & Beloch, 1996; Zhang, Ross, & Davidson, 2004). Anxiety disorders create an enormous burden on society, with annual costs estimated at $42.3 billion, or $1,542 per individual meeting the criteria for an anxiety disorder (Greenberg et al., 1999). Clearly, these disorders are common and substantially interfere with quality of life (Olatunji, Cisler, & Tolin, 2007).

DESCRIPTION OF THE DISORDER

Panic Disorder

Panic attacks are defined as discrete periods of intense fear or discomfort that begin abruptly and reach their peak within 10 minutes. The *DSM-5* requires that at least 4 of the following 13 symptoms be present: palpitations, pounding heart, or accelerated heart rate; sweating; trembling or shaking; sensations of shortness of breath or smothering; feelings of choking; chest pain or discomfort; nausea or abdominal distress; feeling dizzy, unsteady, lightheaded, or faint; derealization or depersonalization; fear of losing control or going crazy; fear of dying; paresthesias; and chills or hot flushes. Panic attacks occur in nonclinical populations, with about 6.3% of a community sample reporting having experienced a full-blown panic attack some time during their lives (Norton, Zvolensky, Bonn-Miller, Cox, & Norton, 2008) without debilitating consequences, development of a disorder, or treatment-seeking behavior.

Panic attacks also occur in the context of many psychiatric conditions, especially anxiety disorders. For example, the acute fear responses that individuals with specific phobias experience in the presence of feared objects or situations (e.g., spider phobics' responses to spiders) sometimes meet the criteria for a panic attack. When a panic attack is triggered by exposure to or anticipation of a feared object or situation, it is considered to be an expected panic attack (also known as a cued panic attack). Expected panic attacks are most common among individuals with other anxiety disorders, including social anxiety disorder and specific phobias.

In addition to expected panic attacks, panic attacks can also be unexpected (or uncued); these panic attacks are not associated with any specific object or situation. Anyone, including individuals with no diagnoses, can experience expected or unexpected panic attacks. Expected panic attacks are not uncommon among individuals with social anxiety disorder or specific phobias, but they also occur in a substantial number of patients with panic disorder (Craske et al., 2010). One issue that should be considered when diagnosing panic disorder is that the term *unexpected* may have different meanings across various cultural contexts (Lewis-Fernández et al., 2010).

The diagnosis of panic disorder requires recurrent and unexpected (uncued) panic attacks, followed by at least 1 month of concern about (a) additional attacks or the implications of the attack, or (b) changes in behavior (APA, 2013). The *DSM-5* does not recognize subtypes of panic disorder (e.g., respiratory, nocturnal, nonfearful, cognitive, and vestibular subtypes), although some investigators have recently explored the possibility of categorizing panic disorder in this way (see Kircanski, Craske, Epstein, & Wittchen, 2010).

Agoraphobia

Agoraphobia is a fear of being in public places or situations in which escape might be difficult or in which help may be unavailable if a panic attack occurred. Patients with agoraphobia avoid (or endure with marked distress) certain situations, including large stores; open or crowded public spaces; traveling on buses, trains, or cars; and being far or away from home (APA, 2013).

The *DSM-III-R* (APA, 1987) viewed agoraphobia as primary and panic attacks as a frequent but secondary feature. It included the diagnostic categories of "agoraphobia with panic attacks" and "agoraphobia without panic attacks." Subsequent revisions of the *DSM* have reversed this view and have included diagnostic categories of "panic disorder with agoraphobia," "panic disorder without agoraphobia," and an infrequently used category of "agoraphobia without panic disorder." This last category is used for patients who deny or have an unclear history of panic attacks, or who merely report histories of panic-like experiences (e.g., limited symptom panic attacks). Such cases may be difficult to differentiate from specific phobias, obsessive-compulsive disorder, and posttraumatic stress disorder. Although agoraphobia was seen as a frequent but secondary feature of panic disorder in the *DSM-III-R* and *DSM-IV*, the view that it is a distinctive condition independent of panic disorder (Wittchen, Gloster, Beesdo-Baum, Fava, & Craske, 2010) is now incorporated into the *DSM-5*.

Generalized Anxiety Disorder

Generalized anxiety disorder (GAD) is characterized by worry (APA, 2013), which is typically defined as repetitive thinking about potential future threat, imagined catastrophes, uncertainties, and risks (Watkins, 2008). Individuals with GAD spend an excessive amount of time worrying and feeling anxious about a variety of topics, and they find it difficult to control the worry. The diagnosis also requires three or more of the following six symptoms: (1) restlessness or feeling keyed up or on edge; (2) being easily fatigued; (3) difficulty concentrating or mind going blank; (4) irritability; (5) muscle tension; and (6) sleep disturbance. Finally, the worry and anxiety are not confined to another disorder (e.g., worry about social evaluation only in the context of social anxiety disorder), and they lead to significant distress or impairment.

The diagnosis of GAD first appeared in the *DSM-III* (APA, 1980), but it was poorly defined, unreliable, and assigned only in the absence of other disorders (Mennin, Heimberg, & Turk, 2004). With publication of the *DSM-III-R* (APA, 1987), the diagnostic criteria for GAD were revised to include worry as the primary feature and to allow for primary diagnoses of GAD in the presence of other disorders. Despite these improvements, diagnostic reliability remained poor due to overly broad criteria for associated symptoms (Marten et al., 1993). The *DSM-IV* (APA, 1994) added the uncontrollability criterion and reduced the set of associated symptoms to reflect empirical findings and to improve specificity. As a result, diagnostic reliability improved but remained low relative to most of the other anxiety disorders (Brown, Di Nardo, Lehman, & Campbell, 2001). The *DSM-5* continues to use the same diagnostic criteria.

Although worry is the primary diagnostic and clinical feature of GAD, the majority of high worriers do not meet criteria for the disorder (Ruscio, 2002). However, compared to high worriers without GAD, high worriers with GAD report greater distress and impairment associated with worry, indicating that worry is more harmful at clinical levels. High worriers with GAD are also more likely to perceive their worry as uncontrollable (Ruscio & Borkovec, 2004). Individuals who do not meet the

"excessiveness of worry" criterion may present a milder form of GAD; they are less symptomatic overall and report fewer comorbid disorders compared to individuals with full GAD (Ruscio et al., 2005). Nonetheless, GAD without "excessive" worry is associated with considerable impairment, high rates of treatment seeking, and high rates of comorbidity.

GAD was initially conceptualized as a "nonphobic anxiety disorder" and was instead classified (alongside panic disorder) under the umbrella of "anxiety neurosis" (*DSM-II*; APA, 1968). Although it remains unclear whether GAD is indeed a "nonphobic" condition in which no specific feared stimulus exists, several theoretical conceptualizations of GAD converge on the idea that worry serves an avoidant function. These conceptualizations include the avoidance theory, the intolerance of uncertainty model, the meta-cognitive model, and emotion regulation models (for a detailed review, see Behar, DiMarco, Hekler, Mohlman, & Staples, 2009).

The avoidance theory (Borkovec, Alcaine, & Behar, 2004) holds that the verbal-linguistic properties of worry preclude emotional processing.Worry is primarily verbal-linguistic as opposed to imagery based in nature (Behar, Zuellig, & Borkovec, 2005; Borkovec & Inz, 1990; Stöber, Tepperwien, & Staak, 2000), and it inhibits somatic arousal during a subsequent anxiety-inducing task (Borkovec & Hu, 1990; Borkovec, Lyonfields, Wiser, & Deihl, 1993; Peasley-Miklus & Vrana, 2000). Moreover, worry is associated with decreased anxious affect during subsequent periods of trauma recall (Behar et al., 2005) and depressive rumination (McLaughlin, Borkovec, & Sibrava, 2007). Lastly, individuals with GAD often report that worry serves as a distraction from more emotional topics (Borkovec & Roemer, 1995). Thus, it seems that worry precludes the somatic and emotional activation required for habituation to anxiety-provoking stimuli. Moreover, worry may be negatively reinforced via the removal of aversive and evocative images and emotional experiences (Borkovec et al., 2004).

Intolerance of uncertainty (IU) is defined as the tendency to respond negatively to uncertain situations in terms of cognition, affect, and behavior (Dugas, Buhr, & Ladouceur, 2004). IU is further defined as a schema through which an individual with GAD perceives the environment; for the individual with GAD, uncertain situations are unacceptable and distressing and may lead to worry (Dugas et al., 2004). Individuals with GAD consistently report greater levels of IU compared to nonclinical controls (Dugas, Gagnon, Ladouceur, & Freeston, 1998; Ladouceur, Blais, Freeston, & Dugas, 1998) and individuals with other anxiety disorders (Dugas, Marchand, & Ladouceur, 2005; Ladouceur et al., 1999). Finally, worry partially statistically mediates the relationship between IU and anxiety (Yook, Kim, Suh, & Lee, 2010).

The premise of the metacognitive model of GAD is that individuals with GAD experience two types of worry: Type 1 worry refers to worry about external threats and noncognitive internal triggers (e.g., physical symptoms), whereas Type 2 worry refers to meta-worry, or worry about worry (Wells, 1995, 2004). Positive beliefs about worry (e.g., that worrying will help avoid a catastrophe) give rise to Type 1 worry, whereas negative beliefs about worry (e.g., the belief that worry is uncontrollable) prompt Type 2 worry. Negative beliefs about worry may be more specific to GAD compared to positive beliefs about worry. Individuals with GAD perceive worry as more dangerous and uncontrollable than do individuals with other anxiety disorders and controls, even when controlling for Type 1 worry (Davis & Valentiner, 2000;

Wells & Carter, 2001). Type 2 worry, on the other hand, may not be specific to GAD; individuals with GAD do not report greater positive beliefs about worry compared to anxious nonworriers (Davis & Valentiner, 2000), high worriers without GAD (Ruscio & Borkovec, 2004), and individuals with other anxiety disorders (Wells & Carter, 2001).

Emotion dysregulation models propose that individuals with GAD have difficulties understanding and modulating their emotions, and they may instead rely on suppression and control strategies (e.g., worry; Mennin, Heimberg, Turk, & Fresco, 2002). The model further describes specific components of emotion dysregulation in GAD, including heightened intensity of emotions (both positive and negative, but particularly negative; Turk, Heimberg, Luterek, Mennin, & Fresco, 2005), poor understanding of emotions, negative reactivity to emotions, and maladaptive management of emotions (Mennin, Heimberg, Turk, & Fresco, 2005; Mennin, Holaway, Fresco, Moore, & Heimberg, 2007). Both analogue and clinical GAD samples report higher emotion dysregulation compared to nonanxious participants, although individuals with depression report similar deficits. Moreover, self-reported emotion dysregulation predicts severity of trait worry and analogue GAD status when controlling for negative affect (Salters-Pedneault, Roemer, Tull, Rucker, & Mennin, 2006), as well as dimensional GAD-Q-IV scores when controlling for symptoms of depression and anxious arousal (Roemer et al., 2009). The acceptance-based model also posits difficulties with emotional experiences in GAD, but instead focuses on fear and avoidance of internal experiences (Roemer, Salters, Raffa, & Orsillo, 2005). Indeed, deficits in mindfulness account for unique variance in GAD symptom severity, even after controlling for emotion regulation and depressive and anxious symptoms (Roemer et al., 2009).

Social Anxiety Disorder

Social anxiety disorder, sometimes referred to as social phobia, is a marked and persistent fear of social or performance situations in which embarrassment may occur. Exposure to or anticipation of the feared social situation almost invariably provokes anxiety or fear. Acute fear responses can take the form of situationally bound or predisposed panic attacks. Feared situations include performing certain activities in the presence of others (such as speaking, eating, drinking, or writing), or fearing that one may do something that will cause humiliation or embarrassment, such as saying something stupid or not knowing what to say, behaving inappropriately, or appearing overly anxious. The diagnosis requires that these feared situations are either avoided or endured with significant distress (APA, 2013). The insight criterion found in prior versions of the *DSM* (i.e., that the individual recognizes that the fear is irrational) has been replaced with the criterion that the clinician judges the fear to be out of proportion to actual danger (APA, 2013). Cultural factors are likely to affect the assessment of this requirement, as it implies a comparison to the patient's social reference group (Lewis-Fernández et al., 2010).

If an individual fears many or most social interactions, the generalized subtype should be specified. Generalized social anxiety disorder overlaps considerably with avoidant personality disorder, "so much so that they may be alternative conceptualizations of the same or similar conditions" (APA, 2000, p. 720). Individuals not

assigned to the generalized subtype are commonly viewed as belonging to a nongeneralized or specific subtype. Compared to the nongeneralized subtype, the generalized subtype is associated with greater comorbidity, earlier age of onset, and greater heritability, and is generally an indicator of greater severity, as is the overlapping diagnosis of avoidant personality disorder (Bögels et al., 2010).

Social anxiety disorder may subsume three other possible disorders. First, the separate diagnostic category of selective mutism may be an expression of social anxiety disorder during childhood (Bögels et al., 2010). This conceptualization of selective mutism treats the refusal to talk as a form of social avoidance. Second, the *DSM-5* recognizes a culturally bound syndrome, Taijin Kyofusho, found mainly in Japan and Korea. The Korean term *Taein-kongpo* is used interchangeably with social anxiety disorder (Kim, personal communication, 2010). These conditions appear to be the same as anthropophobia, a condition recognized in the ICD-10 (World Health Organization, 1992). These conditions involve a fear of offending and making others uncomfortable, such as through poor manners or bad odors, and have also been documented in Western cultures (Kim, Rapee, & Gaston, 2008; McNally, Cassiday, & Calamari, 1990). Lewis-Fernández et al. (2010) have suggested that the definition of social anxiety disorder could be broadened to subsume Taijin Kyofusho and equivalent conditions. Third, the *DSM-5* does not recognize test anxiety as a separate disorder but subsumes it within social anxiety disorder. LeBeau et al. (2010) suggested that one form of test anxiety may be a form of social anxiety disorder in that it involves social evaluative concerns and acute fear reactions, whereas a second form may be a form of generalized anxiety disorder in that it involves anticipatory anxiety and worry. The *DSM-5* requires a specification when "performance anxiety only" applies, implying that there may be two distinct conditions within the diagnostic category of social anxiety disorder.

SPECIFIC PHOBIAS

Specific phobias are marked and persistent fears of clearly discernible, circumscribed objects or situations. Exposure or anticipation of exposure to the feared object or situation almost invariably provokes anxiety or fear. Acute fear responses can take the form of expected (situationally bound or cued) panic attacks. Five subtypes of specific phobia are recognized by the *DSM-5* and are specified based on the type of object or situation that is feared: animals (e.g., dogs, snakes, spiders), natural environment (e.g., storms, water, heights), blood-injection-injury (BII; e.g., seeing blood, getting an injection with a syringe), situations (e.g., elevators, flying), and other (e.g., situations related to choking, vomiting, illness, falling without means of physical support). The diagnosis requires that these feared situations are either avoided or endured with significant distress (APA, 2013).

Although many individuals meet criteria for a specific phobia, very few seek treatment (Barlow, DiNardo, Vermilyea, Vermilyea, & Blanchard, 1986), although individuals with comorbid diagnoses might be more likely to seek treatment (Barlow, 1988). Animal phobia and height phobia are the most frequently diagnosed forms (Curtis, Magee, Eaton, Wittchen, & Kessler, 1998; Stinson et al., 2007). Although subtypes of specific phobia appear to have relatively distinctive ages of onset (Öst, 1987), they are generally accepted as constituting a single category. An exception is

that the BII subtype may be or may subsume a disorder with distinct features and etiological factors (LeBeau et al., 2010; Page, 1994).

Diagnostic Considerations

Anxiety disorders identified in the *DSM-5* show considerable overlap and high rates of comorbidity. These observations suggest that a categorical approach to understanding these problems is not optimal. In addition, these problems do not appear to be discontinuous from normal (nonclinical) variation. Dimensional methods may more accurately model the nature of these problems (Krueger, 1999; Watson, 2005) and may eventually come into use. Given the usefulness of the diagnostic categories of panic disorder, GAD, social anxiety disorder, and specific phobias, it is not surprising that the definitions of these diagnoses have not changed substantially since the publication of the *DSM-III-R*.

One model for organizing internalizing problems involves distinguishing between distress and fear disorders (Krueger, 1999; Watson, 2005). Panic disorder and specific phobias involve acute fear reactions and avoidance behaviors that occur in response to specific stimuli. In panic disorder, the feared stimulus is an internal physiological sensation, such as a racing heart or dizziness. Each subtype of specific phobia is cued by a class of feared stimuli (e.g., snakes, heights). These fear disorders can be distinguished from distress disorders that include major depressive disorder, GAD, and other internalizing disorders not characterized by an acute fear response.

The anxiety associated with GAD does not appear to occur in response to specific feared stimuli, but rather can be thought of as "anxious expectation" (APA, 2013). Elsewhere it has been described as "a chain of thoughts and images, negatively affect-laden and relatively uncontrollable; it is an attempt to engage in mental problem-solving on an issue whose outcome is uncertain but contains the possibility of one or more negative outcomes" (Borkovec, Robinson, Pruzinsky, & DePree, 1983; p. 10). Interpersonal concerns are the most commonly reported worry topic, regardless of GAD status (Roemer, Molina, & Borkovec, 1997). However, individuals with GAD are more likely than those without GAD to worry about minor or routine issues, as well as health or illness (Craske, Rapee, Jackel, & Barlow, 1989; Roemer, Molina, Litz, & Borkovec, 1997). They also report more worry topics overall and that their worry is less controllable and more realistic. Finally, although the diagnosis of GAD is categorical, taxometric analyses have indicated that worry exists on a continuum and may occur to a greater or lesser extent in a given individual (Olatunji, Broman-Fulks, Bergman, Green, & Zlomke, 2010; Ruscio, Borkovec, & Ruscio, 2001). Given that worry is the core diagnostic feature of GAD, these findings support a dimensional classification of the disorder.

Although many of the physiological symptoms of GAD overlap with depression, the *DSM-5* criteria for GAD include those symptoms that show unique associations with worry after controlling for depression. These symptoms include muscle tension (Joormann & Stöber, 1999), gastrointestinal symptoms, and aches and pains (Aldao, Mennin, Linardatos, & Fresco, 2010).

Watson (2005) found that social anxiety disorder shows closer relationships with depression and GAD than it does with panic disorder, suggesting that it might be

conceptualized as a distress disorder. However, for the nongeneralized subtype, acute fear reactions (including cued panic attacks) are often triggered by social situations, such as having to give a speech to an audience. Thus, generalized social anxiety disorder may be a distress disorder, whereas the nongeneralized subtype may be a fear disorder (Carter & Wu, 2010).

Although the *DSM-5* does not recognize higher-order classes of distress and fear disorders, there is good evidence for these superordinate classes because of patterns of comorbidity or co-occurrence of symptoms and patterns of shared heritable risk (Krueger, 1999). Presence (versus absence) of an acute fear response and avoidance behavior may be the key diagnostic distinction for fear disorders (versus distress disorders). Differential diagnosis within the fear disorder category (e.g., panic disorder versus animal phobia versus natural environment phobia) requires identification of the feared stimuli. For example, if panic attacks only occur upon exposure to or anticipation of a specific stimulus, then panic disorder is not indicated and the specific stimulus provides a clue as to the subtype of specific phobia that best describes the condition.

Despite such questions about the best way to conceptualize these types of problems, the *DSM-5* categories have proven to be quite useful, especially with regard to predicting prognosis and treatment response. These disorders are quite recognizable, with relatively good reliability of diagnosis when using a semistructured interview (Brown, Campbell, Lehman, Grisham, & Mancill, 2001). Additionally, given the availability of a host of treatment manuals, treatment planning is greatly facilitated when working with patients seeking treatment for panic disorder, GAD, social anxiety disorder, or specific phobias. Finally, it should be noted that anxiety disorders present risk of suicide, especially when comorbid diagnoses (e.g., depression, personality disorders) are present (Cox, Direnfeld, Swinson, & Norton, 1994; Khan, Leventhal, Khan, & Brown, 2002; Warshaw, Dolan, & Keller, 2000).

EPIDEMIOLOGY

PANIC DISORDER

Prevalence The lifetime prevalence rate of panic disorder with agoraphobia is estimated to be between approximately 1.5% and 5%, whereas the 12-month prevalence rate is estimated to be between approximately 1% and 2.7% (Barlow, 2002; Grant et al., 2006; Kessler, Berglund et al., 2005; Kessler, Chiu, Demler, & Walters, 2005).

Gender The incidence rate of panic disorder is approximately 2 times higher in women than in men (Barlow, 2002; Bland, Orn, & Newman, 1988; Mathews, Gelder, & Johnson, 1981; Wittchen, Essau, von Zerssen, Krieg, & Zaudig, 1992). Different hypotheses have been proposed to account for observed gender differences in relation to the incidence of panic disorder. For example, it is possible that women are simply more likely to report fear, or it is possible that men are more likely than women to engage in self-medication for their anxiety and, thus, are less likely to report problems with panic (Barlow, 2002). The gender distribution of panic disorder with agoraphobia is even more unbalanced, with the greater incidence in women again potentially being due to gender role socialization (Bekker, 1996).

Age of Onset The average age of onset for panic disorder is 26.5 years of age (range = 19.7 – 32) (Burke, Burke, Regier, & Rae, 1990; Grant et al., 2006; McNally, 2001; Öst, 1987). Panic disorder typically first appears during adulthood, although it also appears in prepubescent children and older adults (Barlow, 2002).

Comorbidity Approximately half of individuals currently suffering from panic disorder also suffer from a comorbid psychological disorder, with comorbidity estimates ranging from 51% to 60% (Brown, Antony, & Barlow, 1995; Brown et al., 2001). Among the most commonly co-occurring disorders, approximately 59% of individuals with panic disorder have a comorbid mood or anxiety disorder and 46% have a comorbid anxiety disorder alone. Among specific disorders, approximately 23% of individuals with panic disorder suffer from co-occurring major depressive disorder, 16% suffer from co-occurring GAD, 15% suffer from co-occurring social anxiety disorder, and 15% suffer from co-occurring specific phobia (Brown et al., 2001). Panic disorder is also often accompanied by substance use disorders (Barlow, 2002), and this comorbidity appears to substantially reflect attempts at self-medication, and, to a lesser degree, common genetic vulnerability (Kushner, Abrams, & Borchardt, 2000).

Clinical Course The clinical course for panic disorder is chronic and disabling without treatment. The 12-month remission rate for panic disorder is estimated to be approximately 17%, and the 5-year remission rate is estimated to be approximately 39% (Keller et al., 1994; Yonkers et al., 1998). Panic disorder is also associated with substantial social, occupational, and physical disability, including especially high rates of medical utilization (Barlow, 2002).

Generalized Anxiety Disorder

Prevalence The lifetime prevalence rate of GAD is 5.7% (Kessler, Berglund et al., 2005), whereas the 12-month prevalence rate is 3.1% (Kessler, Chiu et al., 2005).

Gender GAD is more prevalent among women compared to men. In a nationally representative sample, women were approximately twice as likely as men to report lifetime and 12-month diagnoses of GAD, and reported greater disability from GAD (Vesga-López et al., 2008). Given that the genetic contribution to GAD is equivalent among men and women, gender differences in prevalence are likely due to cognitive and environmental influences (Hettema, Prescott, & Kendler, 2001). Finally, although prevalence and severity differ between genders, rates of relapse and remission are similar (Yonkers, Bruce, Dyck, & Keller, 2003).

Age of Onset GAD is associated with a later age of onset compared to the other anxiety disorders, with 50% of lifetime cases beginning by age 31 (Kessler, Berglund, et al., 2005). This later age of onset may reflect the fact that the symptoms of GAD and associated impairment are recognized later during the course of the disorder.

Comorbidity Correctly classifying GAD may be particularly difficult due to high rates of comorbidity and symptom overlap with other disorders, especially major depressive disorder (Kessler, Chiu, et al., 2005). Twenty-six percent of those with a primary

diagnosis of GAD also meet criteria for current major depressive disorder (Brown, et al., 2001). Moreover, when disregarding the *DSM-IV* hierarchy rule that prohibits the diagnosis of GAD when symptoms occur only during the course of a mood disorder, 67% of those with a primary diagnosis of major depressive disorder also meet diagnostic criteria for current GAD. In a longitudinal birth-cohort study, Moffitt et al. (2007) found that 12% of the sample had lifetime diagnoses of both GAD and major depressive disorder. Among those comorbid cases, 37% reported that GAD temporally preceded major depressive disorder, whereas 32% reported that major depressive disorder temporally preceded GAD.

Despite substantial comorbidity between GAD and major depressive disorder, a recent study found evidence that GAD was more similar to other anxiety disorders than it was to depression with respect to risk factors and temporal patterns (Beesdo, Pine, Lieb, & Wittchen, 2010). Furthermore, a substantial proportion of GAD diagnoses occur without comorbid depression, and levels of impairment between the two disorders are comparable (Kessler, DuPont, Berglund, & Wittchen, 1999). Thus, although GAD and major depressive disorder overlap considerably, evidence suggests that they occur independently and likely represent unique syndromes.

Clinical Course A naturalistic longitudinal study found that 42% of participants who had GAD at baseline were still symptomatic at 12-year follow-up (Bruce et al., 2005). Although cognitive-behavioral therapy is effective for treating GAD (Borkovec & Ruscio, 2001) and reducing symptoms of comorbid Axis I disorders (Borkovec, Abel, & Newman, 1995), only 50% of patients achieve high end-state functioning as a result of treatment (Borkovec, Newman, Pincus, & Lytle, 2002).

SOCIAL ANXIETY DISORDER

Prevalence The lifetime prevalence rate of social anxiety disorder is estimated to be between 5.0% and 13.3%, whereas the 12-month prevalence rate is estimated to be between 2.8% and 6.8% (Grant et al., 2005; Kessler et al., 1994; Kessler, Berglund, et al., 2005; Kessler, Chiu, et al., 2005).

Gender The incidence rate of social anxiety disorder is relatively equally represented between genders, with the sex ratio (1.4:1) only somewhat favoring women relative to men (Kessler, Berglund, et al., 2005).

Age of Onset The average age of onset for social anxiety disorder is approximately 15 years of age, with a median age of onset of approximately 12.5 years of age (Grant et al., 2005). Social anxiety disorder is typically especially prevalent among young adults between the ages of 18 and 29 (Kessler, Berglund, et al., 2005).

Comorbidity Approximately 46% of individuals currently suffering from social anxiety disorder also suffer from a comorbid Axis I disorder (Brown et al., 2001). Among the most commonly co-occurring disorders, approximately 45% of individuals with social anxiety disorder have a comorbid mood or anxiety disorder, and approximately 28% of individuals have a comorbid anxiety disorder alone. Among specific disorders, approximately 14% of individuals with social anxiety disorder suffer from

co-occurring major depressive disorder, and 13% of individuals suffer from co-occurring GAD (Brown et al., 2001). Other commonly comorbid disorders include substance use disorders (Grant et al., 2005).

Clinical Course The clinical course for social anxiety disorder is chronic and disabling without treatment. The 12-month remission rate for social anxiety disorder is estimated to be approximately 7%, and the 5-year remission rate is estimated to be approximately 27% (Yonkers, Bruce, Dyck, & Keller, 2003). Social anxiety disorder is also associated with substantial social, occupational, and physical disability, including especially high levels of scholastic difficulties (Stein & Kean, 2000).

Specific Phobia

Prevalence The lifetime prevalence rate for specific phobia is estimated to be between 2% and 12.5%, whereas the 12-month prevalence rate is estimated to be between 1.8% and 8.7% (Bland et al., 1988; Eaton, Dryman, & Weissman, 1991; Kessler, Berglund, et al., 2005; Kessler, Chiu, et al., 2005; Lindal & Stefansson, 1993; Stinson et al., 2007; Wittchen, Nelson, & Lachner, 1998). Among the specific phobias, animal phobia and height phobia are the most frequently diagnosed forms (Curtis et al., 1998; Stinson et al., 2007).

Gender Specific phobia is approximately 4 times more common in women than in men (Kessler, Berglund, et al., 2005). However, research indicates that the incidence of phobias of heights, flying, injections, dentists, and injury do not significantly differ between women and men (Fredrikson, Annas, Fischer, & Wik, 1996). Different hypotheses have been put forth to account for observed gender differences in relation to the incidence of specific phobia. These hypotheses include differences relating to the reporting of fear between genders, as well as differences in the ways women and men are taught to deal with threatening stimuli (Barlow, 2002).

Age of Onset The average age of onset for specific phobia is between 9.1 and 16.1 years of age (Stinson et al., 2007; Thyer, Parrish, Curtis, Nesse, & Cameron, 1985), with a median age of onset of approximately 15 years (Magee, Eaton, Wittchen, McGonagle, & Kessler, 1996). Moreover, results suggest that particular specific phobias may have differential ages of onset. For example, animal phobia and BII phobia tend to begin in childhood, whereas situational phobia and height phobia tend to develop in adolescence or adulthood (e.g., Antony, Brown, & Barlow, 1997; Barlow, 2002; Himle, McPhee, Cameron, & Curtis, 1989; Marks & Gelder, 1966; Öst, 1987).

Comorbidity Specific phobias are likely to co-occur with other specific phobias, with only 24.4% of phobic individuals having a single specific phobia (Curtis et al., 1998). However, other findings suggest that the presence of multiple specific phobias is relatively rare (Fredrikson et al., 1996). Moreover, approximately 34% of individuals currently suffering from a specific phobia meet the criteria for an additional Axis I disorder, with mood and anxiety disorders being the most common co-occurring disorders (Brown et al., 2001). Among mood and anxiety disorders, some research has found especially high rates of co-occurring panic disorder in individuals suffering

from specific phobias (Stinson et al., 2007). Other data suggest that specific phobias are rarely the principle diagnosis when they co-occur with other disorders, but they are often a secondary diagnosis (Barlow, 2002; Sanderson, Di Nardo, Rapee, & Barlow, 1990).

Clinical Course The clinical course for specific phobia is relatively chronic and disabling without treatment. The 15-month full remission rate is estimated to be approximately 19% (Trumpf, Becker, Vriends, Meyer, & Margraf, 2009). Specific phobia is also often associated with substantial social, occupational, and physical disability, including avoidance of medical procedures (Wolitzky-Taylor, Horowitz, Powers, & Telch, 2008).

TREATMENT

PHARMACOLOGICAL TREATMENTS

Panic Disorder Many pharmacological agents have been used for the treatment of panic disorder with and without agoraphobia, including benzodiazepines, selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs), and tricyclic antidepressants (e.g., Ballenger et al., 1988; Barlow, Gorman, Shear, & Woods, 2000; Marks et al., 1993; Mavissakalian & Perel, 1999; Tesar et al., 1991; van Vliet, Westenberg, & den Boer, 1993). Among these agents, a growing body of research suggests that SSRIs and SNRIs should be considered the front-line pharmacological agents for the treatment of panic disorder (Hoffman & Mathew, 2008; McHugh, Smits, & Otto, 2009; Pollack et al., 2007). Although benzodiazepines have been shown to be effective in the treatment of panic, they are associated with abuse potential and may interfere with psychological interventions; specifically, they interfere with the experience of anxiety during exposure to feared situations (Jorstad-Stein & Heimberg, 2009) and are thus not considered first-line pharmacological agents for panic disorder.

Generalized Anxiety Disorder A host of pharmacological interventions have been used in the treatment of GAD, including benzodiazepines, SSRIs, SNRIs, tricyclic antidepressants, Buspirone, and Pregabalin (Baldwin, Waldman, & Allgulander, 2011; Hidalgo, Tupler, & Davidson, 2007; Katzman, 2009; Mitte, Noack, Steil, & Hautzinger, 2005; Mula, Pini, & Cassano, 2007; Rickels & Rynn, 2002). When GAD is comorbid with depression, SSRIs and tricyclic antidepressants may evidence greater efficacy relative to benzodiazepines (Davidson, 2009) by targeting symptoms of both GAD and depression uniquely (Olatunji et al., 2008). It should be noted that benzodiazepines may be associated with high dropout rates (Martin et al., 2007). Furthermore, because benzodiazepines, tricyclic antidepressants, and SSRIs are associated with adverse side effects that may limit their utility, Buspirone and Pregabalin are often relied upon as first-line pharmacological treatments for GAD (Mitte et al., 2005).

Social Anxiety Disorder Efficacious pharmacological agents for the treatment of social anxiety disorder include benzodiazepines, SSRIs, SNRIs, and MAOIs (e.g., Blackmore, Erwin, Heimberg, Magee, & Fresco, 2009; Blanco et al., 2003; Clark et al., 2003;

Davidson et al., 2004; Gerlernter et al., 1991; Kobak, Greist, Jefferson, & Katzelnick, 2002; Ledley & Heimberg, 2005; Otto et al., 2000). Given the noted concerns surrounding benzodiazepines, the SSRIs, SNRIs, and MAOIs are considered the first-line pharmacological agents for the treatment of social anxiety disorder (Jorstad-Stein & Heimberg, 2009).

Specific Phobia Extant data suggest that use of pharmacological agents, such as benzodiazepines and sedatives, in the treatment of specific phobias is limited. Moreover, there exists a paucity of data relating to the efficacy of antidepressant medications as they relate to the treatment of specific phobias (Grös & Antony, 2006; Hamm, 2009). Pharmacological agents are not standard treatments for specific phobias, and many individuals with specific phobia do not seek treatment, likely managing their fears using avoidance and self-medication (Bandelow et al., 2012).

Cognitive-Behavioral Treatments

Panic Disorder Often considered to be a first-line treatment, cognitive-behavioral therapy (CBT) that incorporates psychoeducation, interoceptive and *in vivo* exposures, and cognitive restructuring has been shown to be efficacious in both individual and group format, with 80% to 90% of patients showing marked improvement (e.g., Barlow et al., 2000; Clark et al., 2003; Hofmann & Smits, 2008; McHugh et al., 2009; Olatunji, Cisler, & Deacon, 2010; Öst, Thulin, & Ramnero, 2004; Penava, Otto, Maki, & Pollack, 1998; Telch et al., 1993). Interoceptive exposures entail provoking feared arousal-related sensations in order to facilitate habituation of fear and disconfirmation of feared catastrophic outcomes of such sensations. Treatment gains associated with CBT for panic disorder have shown excellent maintenance, including at 2 years posttreatment (e.g., Craske, Brown, & Barlow, 1991).

Generalized Anxiety Disorder Cognitive-behavioral therapy for GAD has also been shown to be efficacious (Borkovec & Ruscio, 2001). Because GAD is not characterized by motoric avoidance of disorder-specific stimuli (as are other anxiety disorders), traditional behavioral exposure techniques that are so effective in the treatment of other anxiety syndromes are not used in the treatment of worry. Instead, approaches to treating GAD rely on targeting nonadaptive patterns of awareness, physiology, behavior, and cognition (Behar & Borkovec, 2005, 2009; Borkovec, Newman, Pincus, & Lytle, 2002; Newman et al., 2011). This approach evidences relatively lower rates of success than do other CBT-based treatments for anxiety, with only 50% of patients reaching high end-state functioning at post-therapy (Borkovec et al., 2002). More recently, an investigation was completed examining the additive value of therapy focusing on interpersonal processes and emotional avoidance above and beyond the effects of CBT; the results of that study failed to indicate that this augmented treatment was associated with superior efficacy relative to CBT alone (Newman et al., 2011).

Social Anxiety Disorder Cognitive-behavioral therapy for social anxiety disorder includes engagement in psychoeducation, exposure to feared social-evaluative situations, and cognitive restructuring in an attempt to modify appraisals and reactions to social situations. Exposures, in which individuals engage in feared social situations,

allow for habituation of fear and disconfirmation of feared catastrophes in the absence of maladaptive responses such as escape and avoidance (e.g., see Clark & Wells, 1995). CBT for social anxiety disorder has been shown to be efficacious in both individual and group formats (Clark et al., 2006; Feske & Chambless, 1995; Heimberg & Becker, 2002; Jorstad-Stein & Heimberg, 2009; Olatunji, Cisler, et al., 2010; Ponniah & Hollon, 2008; Powers, Sigmarsson, & Emmelkamp, 2008). Moreover, treatment gains associated with CBT for social anxiety disorder show excellent maintenance, including at 5 years posttreatment (e.g., Heimberg, Salzman, Holt, & Blendell, 1993). Newer formulations of CBT (e.g., Clark, 2001; Clark & Wells, 1995; Hofmann & Otto, 2008) incorporate manipulation of self-focused attention, elimination of safety behaviors, reevaluation of social costs, and change in self-perceptions.

Specific Phobia Cognitive-behavioral therapy for specific phobia typically involves exposure to feared stimuli. In the absence of avoidance responses, such exposure allows for habituation of fear and disconfirmation of the expected catastrophes associated with coming into contact with feared stimuli (e.g., see Antony & Swinson, 2000). Cognitive-behavioral treatments for specific phobia have been shown to be efficacious (e.g., Choy, Fyer, & Lipsitz, 2007; Hamm, 2009; Muhlberger, Herrmann, Wiedemann, Ellgring, & Pauli, 2001; Olatunji, Cisler, et al., 2010; Öst, 1989; Rothbaum, Hodges, Smith, Lee, & Price, 2000; Van Gerwen, Spinhoven, Diekstra, & Van Dyck, 2002; Wolitzky-Taylor et al., 2008). One version of this treatment, delivered during a single session lasting 2 to 4 hours, has been shown to be highly effective, with about 90% of patients showing marked improvement (Öst, 1989). Treatment gains associated with CBT for specific phobia have shown excellent maintenance, including at 14 months posttreatment (e.g., Choy et al., 2007).

Other Psychological Treatments

Acceptance and commitment therapy (ACT; Hayes, Luoma, Bond, Masuda, & Lillis, 2006) is another psychological treatment for anxiety disorders that has garnered recent interest. Broadly speaking, ACT seeks to reduce the extent to which individuals respond to thoughts and other inner experiences in ways that maintain and exacerbate emotional distress. Preliminary data indicate that ACT is an efficacious treatment for reducing anxiety symptoms (e.g., see Öst, 2008). Moreover, ACT-based treatments for panic disorder (Lopez & Salas, 2009) and social anxiety disorder (Dalrymple & Herbert, 2007) have been examined.

Mindfulness-based approaches have also received attention recently, particularly in the treatment of GAD. Mindfulness is defined as "paying attention in a particular way, on purpose, in the present moment, and nonjudgmentally" (Kabat-Zinn, 1994, p. 4) and "bringing one's complete attention to the present experience on a moment-to-moment basis" (Marlatt & Kristeller, 1999, p. 68). Thus, mindfulness-based treatments for GAD aim to increase clients' awareness and acceptance through practicing mindfulness of internal and external experiences, nonjudgmental observation of those experiences, relaxation, meditation, and a focus on the present moment (Roemer, Salters-Pedneault, & Orsillo, 2006). Mindfulness-based interventions have been shown to be efficacious as stand-alone treatments (e.g., Roemer,

Orsillo, & Salters-Pedneault, 2008), and can also be added to traditional CBT techniques (Behar, Goldwin, & Borkovec, in press) in an attempt to increase efficacy.

Other psychological treatments that have garnered some interest in the treatment of panic disorder, GAD, social anxiety disorder, and specific phobias include interpersonal therapy, psychoanalytic psychotherapy, and eye movement desensitization and reprocessing (EMDR) therapy. High-quality randomized and controlled clinical trials have generally not yet been conducted, or have found no support for treating these disorders with these alternate psychological approaches. For example, an examination of the efficacy of EMDR in the treatment of panic disorder with agoraphobia indicated that EMDR was not significantly different from a credible attention placebo condition (e.g., Goldstein, de Beurs, Chambless, & Wilson, 2000). These treatments are, therefore, not widely considered to be first-line treatments (Hamm, 2009; Jorstad-Stein & Heimberg, 2009; McHugh et al., 2009).

Combined Pharmacological and Psychological Treatments

Traditional Pharmacological Agents Several studies have examined the combined effects of traditional pharmacological agents and cognitive-behavioral treatments for panic disorder (e.g., Azhar, 2000; Barlow et al., 2000; Berger et al., 2004; Spinhoven, Onstein, Klinkhamer, Knoppert-van der Klein, 1996; Stein, Norton, Walker, Chartier, & Graham, 2000). In a review of such studies, Furukawa, Watanabe, and Churchill (2006) concluded that combined traditional pharmacological and psychological treatments in the treatment of panic disorder is modestly more efficacious relative to either pharmacological treatment or CBT for panic disorder alone. However, such a combined approach is associated with greater dropouts and side effects relative to CBT alone for panic disorder (e.g., Barlow et al., 2000).

Likewise, only a few investigations have examined the efficacy of a combined treatment approach for GAD. Power et al. (1990) failed to find superiority of a combined CBT+diazepam approach over CBT-alone, and Crits-Cristoph et al. (2011) failed to find superiority of a combined CBT+venlafaxine approach over venlafaxine-alone, suggesting that combination treatments are not superior to monotherapies in the treatment of GAD.

Only a few known studies have examined whether a combined approach is efficacious for social anxiety disorder. Such findings have been mixed: One study found that a combined approach was superior to a psychological approach alone and pharmacological treatment alone (Blanco et al., 2010), one study found that a combined approach was not superior to a psychological approach alone or a pharmacological approach alone (Davidson et al., 2004), and one study found the psychological treatment alone to be especially beneficial at 1-year follow-up (Blomhoff et al., 2001).

No known studies have examined the efficacy of a combined approach in the treatment of specific phobias, although advantages of such an approach have been posited (e.g., Cottraux, 2004). Some researchers view the use of medications, particularly benzodiazepines, as antithetical to the mechanisms of change in CBT if they are used to reduce feared somatic sensations (Bruce, Spiegel, & Hegel, 1999; Deacon & Abramowitz, 2005).

D-cycloserine (DCS) and Related Issues Among nontraditional pharmacological agents, D-cycloserine (DCS) has emerged as a potentially important supplement to traditional cognitive-behavioral treatments for panic disorder, social anxiety disorder, and specific phobias. DCS, an NMDA agonist, seems to augment learning and memory (Schwartz, Hashtroudi, Herting, Schwartz, & Deutsch, 1996; Tsai, Falk, Gunther, & Coyle, 1999) and has been shown to facilitate conditioned fear extinction in animal studies (Ledgerwood, Richardson, & Cranney, 2003; Walker, Ressler, Lu, & Davis, 2000). Such evidence led investigators to examine whether DCS might enhance the effects of exposure-based cognitive-behavioral interventions in a host of anxiety disorders (e.g., Guastella et al., 2008; Hofmann et al., 2006; Norberg, Krystal, & Tolin, 2008; Ressler et al., 2004). Thus far, evidence indicates that DCS does indeed enhance the effects of CBT for panic disorder, social anxiety disorder, and specific phobias at posttreatment and follow-up; its potential enhancing effects in the treatment of GAD have not been explored.

Behavioral treatments for most anxiety disorders utilize procedures that incorporate exposure to conditioned stimuli, an approach that mirrors the process of fear extinction as studied most extensively in rats. As laboratory investigations using animal models identify agents and procedures that enhance extinction processes, translational applications of these findings to research on humans will hopefully lead to innovative changes to behavior therapy protocols that are used for panic disorder, GAD, social anxiety disorder, and specific phobias. For example, extinction has traditionally entailed learning of safety associations that compete with fear associations; however, alternate procedures might be used to *erase* fear associations altogether, such as through specific chemical agents or behavioral procedures that interfere with reconsolidation (see Quirk et al., 2010). In addition, such research may lead to knowledge regarding the degree to which factors such as sleep and timing between therapy sessions might influence therapeutic effectiveness.

PREDICTORS OF TREATMENT OUTCOME

A host of variables may predict enhanced or compromised response to treatment across anxiety disorders. One commonly examined predictor of treatment outcome is symptom severity. In panic disorder, higher levels of agoraphobia are associated with poorer treatment outcome (e.g., Cowley, Flick, & Roy-Byrne, 1996; Warshaw, Massion, Shea, Allsworth, & Keller, 1997). However, in GAD, the evidence is mixed. Some investigations have shown that patients with more severe anxiety at pretreatment respond less well to therapy (Butler, 1993; Butler & Anastasiades, 1988; Yonkers, Dyck, Warshaw, & Keller, 2000), whereas others have failed to find such relationships (e.g., Barlow, Rapee, & Brown, 1992; Biswas & Chattopadhyay, 2001; Durham, Allan, & Hackett, 1997). In social anxiety disorder, greater severity of depression and greater severity of avoidant personality traits are related to poorer treatment outcome (Chambless, Tran, & Glass, 1997).

Overall, there are mixed findings regarding the impact of comorbid conditions on treatment outcome. For example, some research indicates that individuals with panic disorder who have comorbid major depressive disorder evidence poorer treatment outcome (Cowley et al., 1996), whereas other research has found that such comorbidity does not negatively impact treatment outcome in panic (McLean, Woody, Taylor, &

Koch, 1998; Tsao, Mystkowski, Zucker, & Craske, 2002). In GAD, the presence of a comorbid Axis I disorder generally (Durham et al., 1997), and comorbid dysthymia or panic disorder specifically (Tyrer, Seivewright, Simmonds, & Johnson, 2001), predict relapse of symptoms. In specific phobias, the presence of additional comorbid anxiety disorders does not seem to affect treatment outcome (Ollendick, Öst, Reuterskiöld, & Costa, 2010).

Interpersonal problems seem to predict a poor response to treatment among individuals with GAD patients. For example, Borkovec et al. (2002) found that interpersonal problems remaining at treatment termination predicted poorer functioning at post-therapy and follow-up assessments. Likewise, personality disorder traits are associated with poorer response to cognitive therapy and self-help treatments among GAD patients (Tyrer, Seivewright, Ferguson, Murphy, & Johnson, 1993).

Finally, several treatment process variables (e.g., therapeutic alliance, treatment compliance) have also been examined as predictors of treatment outcome. The degree to which patients expect to change seems to be especially important (Jorstad-Stein & Heimberg, 2009). For example, research indicates that lower levels of treatment expectancy are related to poorer outcome in social anxiety disorder (Chambless et al., 1997).

ASSESSMENT

Multimodal approaches are generally recommended in the assessment of panic disorder, GAD, social anxiety disorder, and specific phobias. These approaches often include the use of a clinical interview, self-report measures, and behavioral tests (e.g., see Antony, 1997; Barlow, 2002; Grös & Antony, 2006). In addition, the emergence of biological assessments may lead to enhanced knowledge of these conditions in the future.

Clinical Interviews

Clinical interviews provide detailed information relating to an individual's psychiatric history and current functioning. Clinical interviews can differ with respect to their format: Some clinical interviews are highly structured and directive, whereas other clinical interviews use an unstructured and conversational approach. When seeking a diagnosis, the use of structured clinical interviews is recommended due to their increased standardization and reliability (Summerfeldt, Kloosterman, & Antony, 2010).

Two of the most commonly used semistructured clinical interviews for diagnosing anxiety disorders include the Anxiety Disorders Interview Schedule for DSM-IV–Lifetime (ADIS-IV-L; Di Nardo, Brown, & Barlow, 1994) and the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID; First, Spitzer, Gibbon, & Williams, 1996). Although these interviews can be used to reach a diagnosis relating to a wide range of psychological disorders, both the ADIS-IV-L and the SCID can also be used to specifically assess whether an individual meets the diagnostic criteria for panic disorder, GAD, social anxiety disorder, or specific phobia. The ADIS-IV-L and the SCID both explicitly provide questions for clinicians to ask when administering the interview. This structured format ensures that each individual is asked the same

questions, in the same order, using the same terminology. However, subsequent questions, which may deviate from the standardized questions, can be used to further probe an individual's presenting problem(s). Both the ADIS-IV-L and the SCID have been shown to have good psychometric properties in prior studies (e.g., see Summerfeldt et al., 2010).

Despite the ADIS-IV-L and the SCID providing a standardized, systematic, and valid assessment of panic disorder, GAD, social anxiety disorder, and specific phobia, both interviews require training and can be time-consuming to administer. Nonetheless, the use of such interviews is recommended when assessing for these three disorders. Inter-rater reliability estimates using the ADIS-IV-L are adequate for GAD ($\kappa = .65$) and good for panic disorder with or without agoraphobia ($\kappa = .79$), social anxiety disorder ($\kappa = .77$), and specific phobia ($\kappa = .71$) (Brown et al., 2001).

SELF-REPORT MEASURES

Self-report measures provide an efficient and cost-effective method to assess for panic disorder, GAD, social anxiety disorder, or specific phobia, as well as their associated symptoms. There are several well-validated self-report measures (see Antony, Orsillo, & Roemer, 2001). We present some of the most commonly used self-report measures to assess each disorder.

For panic disorder, well-validated and frequently used self-report measures include the Panic Disorder Severity Scale (PDSS; Shear et al., 1997) and the Panic and Agoraphobia Scale (PAS; Bandelow, 1999). The Agoraphobic Cognitions Questionnaire (ACQ; Chambless, Caputo, Bright, & Gallagher, 1984) and the Anxiety Sensitivity Index-3 (ASI-3; Taylor et al., 2007) are two frequently used measures to assess for panic-related cognitions and anxiety focused on physical sensations, respectively.

For GAD, the most commonly used self-report measure is the Generalized Anxiety Disorder Questionnaire—DSM-IV (GAD-Q-IV; Newman et al., 2002). The GAD-Q-IV is a nine-item self-report measure of the symptoms of GAD as outlined in the *DSM-IV-TR* and *DSM-5*. Trait worry, the central symptom dimension underlying generalized anxiety disorder, can also be assessed with existing self-report measures, most notably the Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990). The PSWQ is a 16-item self-report trait measure of the frequency and intensity of worry. The PSWQ has demonstrated high internal consistency and good retest reliability (Meyer et al., 1990), correlates well with diagnostic measures of GAD (Behar, Zuellig, & Borkovec, 2005), is distinct from anxiety and depression in clinical samples (Meyer et al., 1990), and discriminates individuals with GAD from those with other anxiety disorders (Brown, Antony, & Barlow, 1992).

For social anxiety disorder, well-validated and frequently used self-report measures include the Social Phobia and Anxiety Inventory (SPAI; Turner, Beidel, Dancu, & Stanley, 1989), the Social Interaction Anxiety Scale (SIAS; Mattick & Clarke, 1998), and the Social Phobia Scale (SPS; Mattick & Clarke, 1998). The Brief Fear of Negative Evaluation Scale (BFNES; Leary, 1983a) is a frequently used self-report measure to assess for the core cognition purported to underlie social anxiety disorder. In addition, the Social Phobia and Anxiety Inventory for Children (SPAI-C; Beidel, Turner,

Hamlin, Morris, 2000) is a well-validated self-report measure for assessing social anxiety symptoms in children and adolescents.

For specific phobias, the Fear Survey Schedule (FSS-II; Geer, 1965) is well validated and commonly used, although other promising self-report measures exist as well (e.g., Phobic Stimuli Response Scales; Cutshall & Watson, 2004). Whereas the FSS-II assesses a broad range of specific phobias, self-report measures designed to assess certain types of specific phobias exist as well (e.g., Fear of Spider Questionnaire [Szymanski & O'Donohue, 1995]; Blood-Injection Symptom Scale [Page, Bennett, Carter, Smith, & Woodmore, 1997). The Spence Child Anxiety Scale (Spence, 1997, 1998; Spence, Barrett, & Turner, 2003) includes both self-report and parent informant versions for assessment of anxiety disorder symptoms in children and adolescents.

Behavioral Assessments

Although less frequently used in clinical practice, behavioral assessment strategies offer unique insights into the nature and expression of an individual's symptoms. The chief goal of behavioral assessments is to evaluate an individual's distress during exposure to and avoidance of his/her feared stimulus. Such an assessment is commonly referred to as a behavioral approach test (BAT). BATs can differ in their orientations, with multiple-task BATs (i.e. BATs that require individuals to complete several fear-related tasks) generally being favored relative to single-task BATs. BATs are idiographic in nature, such that the feared stimulus is chosen based on an individual's specific symptom profile. For example, an individual with spider phobia would likely be exposed to different stimuli relating to spiders, whereas an individual with social anxiety disorder would likely be exposed to situations relating to social or performance situations. In the case of panic disorder, behavioral assessments include physiological symptom inductions that trigger anxiety or fear. Subjective units of distress are often assessed during BATs, with higher units indicating higher levels of distress (e.g., Antony, 1997; Barlow, 2002; Grös & Antony, 2006).

Self-monitoring is another behavioral assessment strategy that is important in the assessment of anxiety disorders. Self-monitoring involves recording thoughts, emotions, and behaviors in response to specific situations. In panic disorder, self-monitoring typically entails recording the time of onset, intensity, antecedents, consequences, and location of panic attacks, as well as cognitions experienced during the attacks. If accompanied by agoraphobia, additional information might include the frequency and duration of excursions from home, distance traveled, escape behaviors, safety behaviors, and level of anxiety (Barlow, 2002).

In GAD, self-monitoring entails recording levels of anxiety and associated behaviors and cognitions at many points throughout the day; the resulting enhanced awareness is then used to help clients catch the anxiety spiral early enough to intervene using prescribed interventions before anxiety becomes excessive (e.g., Behar & Borkovec, 2005, 2009). In social anxiety disorder, self-monitoring typically includes recording the frequency and duration of social interactions, antecedents and consequences of these interactions, cognitions during the interactions, and level of anxiety experienced (e.g., Heimberg, Madsen, Montgomery, & McNabb, 1980). In specific phobia, self-monitoring entails recording thoughts, behaviors, and fear levels upon coming into contact with the feared stimulus.

Despite the potentially useful information that accompanies behavioral assessment strategies, it is important to note that such strategies have been broadly criticized for poorer reliability and validity relative to structured clinical interviews and self-report measures. Moreover, behavioral assessment strategies can be prone to bias (e.g., observer bias, confirmation bias; Groth-Marnat, 2003). In addition to having potential assessment value, self-monitoring may also have therapeutic value by helping individuals become more aware of the automatic cognitions and behaviors that maintain their disorders.

BIOLOGICAL ASSESSMENT

Neuroanatomical differences are not sufficiently established to warrant routine assessment of neuroanatomy in individuals suffering from panic disorder, GAD, social anxiety disorder, and specific phobia (e.g., Britton & Rauch, 2009). Although their diagnostic value is limited at present, neuroanatomical assessment techniques are a promising area of research. Approaches used to assess the neuroanatomy of individuals suffering from panic disorder, GAD, social anxiety disorder, and specific phobias, as well as psychopathology more broadly, can be divided into two different methods: structural (anatomical) techniques and functional (physiological/neurochemical) techniques.

Computerized tomography (CT) and magnetic resonance imaging (MRI) are two of the most common structural techniques used to examine how various parts of the brain relate to one another spatially. Of these two techniques, MRI produces better resolution than does CT and is thus used more often. The most commonly used functional techniques include single photon emission computed tomography (SPECT), functional MRI (fMRI), and positron emission tomography (PET). Such functional techniques allow for the examination of changes in the brain's metabolism and blood flow.

Both SPECT and PET use trace amounts of ligands that are labeled with radioactive isotopes, which in turn allow measurement of cerebral metabolism or cerebral blood flow. This radioactive dye is injected into the bloodstream, and SPECT or PET scanners detect the radiation emitted by the isotopes. PET allows for more precision and better resolution than does SPECT and is thus used more often. fMRI assesses cerebral blood flow in a similar fashion as the other two functional techniques, but fMRI has the advantage of not requiring any exposure to ionizing radiation. It is also important to note that structural and functional methods can be combined, such that a functional image can be placed on top of a structural image (i.e., image registration) to determine the exact structural location of the functional change (Andreasen, 2001).

ETIOLOGY

BEHAVIORAL GENETICS

Behavioral genetic studies (e.g., studies of identical twins, studies of adopted siblings) estimate that about 20% of the variance in panic disorder, social anxiety disorder, and specific phobias is attributable to genetic factors (e.g., Hettema, Neale, Myers, Prescott, & Kendler, 2006). Familial factors (i.e. environmental factors shared by twins

and siblings) account for less than 10% of the variance in the occurrence of the disorders, and the majority of the variance (perhaps as much as 70%) is attributed to unique environmental factors and measurement error. Although some behavioral genetics studies have resulted in higher estimates of the contribution of heritable genetics (perhaps as high as about 50% when correcting for measurement error; Kendler, Karkowski, & Prescott, 1999; Kendler, Myers, Prescott, & Neale, 2001), it is generally agreed that compared to most other psychological conditions, these anxiety disorders appear to be relatively less influenced by heritable genetics and more influenced by environment or by gene-environment interactions. A notable exception to these findings is that the BII subtype of specific phobia appears to be relatively more heritable (Kendler et al., 1999, 2001). In addition, when social anxiety disorder subtypes are examined, the generalized subtype appears to involve somewhat greater heritable genetic risk than the nongeneralized subtype (Mannuzza et al., 1995; Stein et al., 1998).

Some of the heritable genetic risk for panic disorder and specific phobias appears to be due to a general factor (perhaps neuroticism; Gray & McNaughton, 2000; Hettema et al., 2006) underlying most internalizing disorders (Krueger, 1999). A substantial part of the heritable genetic risk is specific to the group of disorders that involves acute fear reactions (Krueger, 1999). A modest amount of disorder-specific heritable genetic risk has been found for panic disorder (Hettema et al., 2006). It is also noteworthy that anxiety sensitivity (Stein, Lang, & Livesley, 1999), which is a risk factor for panic disorder (see Personality and Temperament: Anxiety Sensitivity), and behavioral inhibition (Hirschfield-Becker, Biederman, & Rosenbaum, 2004), which is a risk factor for social anxiety disorder (see Personality and Temperament: Behavioral Inhibition and Shy Temperament), are heritable. Although the largest portion of heritable genetic risk appears to involve a general factor underlying the entire class of disorders that involve acute fear reactions, unique environmental factors appear to play a considerable role, particularly with regard to which type of acute fear disorder develops.

A meta-analysis of family and twin studies found that genetic factors account for approximately 32% of the variance in liability to GAD (Hettema, Neale, & Kendler, 2001). Not surprisingly, there is considerable overlap in genetic liability for GAD and major depressive disorder, 25% of which is accounted for by neuroticism (Kendler, Gardner, Gatz, & Pedersen, 2007). Furthermore, a large twin study found that GAD and depression were linked to one genetic factor termed "anxious-misery," whereas the phobias were linked to another factor termed "fear" (panic disorder was linked to both factors, but less strongly; Kendler, Prescott, Myers, & Neale, 2003). A similar study examining only anxiety disorders found that GAD is linked to the same genetic factor as panic disorder and agoraphobia, whereas a different genetic factor was associated with situational and animal phobias (Hettema, Prescott, Myers, Neale, & Kendler, 2005). Despite genetic overlap, family studies suggest that GAD and panic disorder are somewhat distinct. For example, rates of GAD are higher among relatives of individuals with GAD compared to relatives of individuals with panic disorder (Noyes et al., 1992; Weissman, 1990).

Biological Considerations

The neuroanatomy, neurochemistry, and endocrinology underlying normal fear processes have been studied extensively (see Meaney, LeDoux, & Liebowitz, 2008).

Normal fear and panic responses are often understood as part of a complex physical system involving neural, endocrinological, circulatory, muscular, and behavioral systems. This fight-or-flight system is designed to prevent or avoid physical danger and harm, and involves a fast and efficient response. Perceptions of immediate danger trigger a cascade of physical reactions that begin in the amygdala, which projects to the hypothalamus. The hypothalamus releases corticotropin-releasing factor (CRF), which triggers the pituitary to release adrenocorticotropic hormone (ACTH), which in turn triggers the adrenal cortex to release hormones, including cortisol. These hormones play a central role in regulating the body's preparation for stress.

The hypothalamus also activates the sympathetic nervous system, resulting in a variety of bodily changes including the release of glucose from the liver; increases in heart rate, breathing, and blood pressure; a pattern of vasodilation and vasoconstriction that increases blood flow to the major muscles; and other changes associated with preparation for the fight-or-flight response.

These physiological changes constitute the physical symptoms of panic attacks. Numbing and tingling in the fingers and toes and sensations in the stomach (nausea) and bladder are sometimes experienced as less blood reaches these nonvital areas; shaking and trembling are by-products of the readiness of the major muscles to expend energy; sweating is release of heat in preparation for physical exertion.

Fear appears to be a preparation for a full panic response and involves a similar, though less dramatic, profile of physiological changes and symptoms. Thus, although we consider panic attacks and acute fear responses in the context of anxiety disorders to reflect pathology, the pathology does not appear to be due to the manner in which the hypothalamic-pituitary-adrenal (HPA) axis system is carrying out its function. Rather, the pathology appears to be due to the inappropriate triggering of the HPA axis, which typically works well to avoid physical danger and harm, even in individuals with panic disorder, social anxiety disorder, and specific phobias.

Consistent with this view, no abnormalities in the cardiovascular and vestibular systems have been consistently established for panic disorder (Jacob, Furman, Durrant, & Turner, 1996; Kathol et al., 1980; Shear, Devereaux, Kranier-Fox, Mann, & Frances, 1984). Anxiety disorders in general do, however, appear to be associated with greater reactivity in the amygdala (see Britton & Rauch, 2009; Meaney et al., 2008). For example, compared to nonanxious controls, children with anxiety disorders have increased amygdala activity when viewing fearful versus neutral faces (Pine et al., 2005). There is evidence that hyperventilation in patients with panic disorder may lead to decreased blood flow and changes in metabolism in and around the hippocampus, but it is not clear whether these observations constitute differential processing compared to nondisordered individuals (Uhde & Singareddy, 2002). Overall, researchers have not identified neuroanatomical or neurochemical features that are specific to panic disorder, social anxiety disorder, or specific phobias (see Britton & Rauch, 2009).

Physiology of GAD is characterized by autonomic inflexibility; chronic tension and anxiety may lead to a restricted range of autonomic responses to environmental triggers (Thayer, Friedman, & Borkovec, 1996). GAD is associated with decreased vagal tone (an index of parasympathetic activity) and heart rate (Lyonfields, Borkovec, & Thayer, 1995; Thayer et al., 1996). Importantly, physiological variables differ among individuals with GAD; only those high in baseline sympathetic arousal

displayed reduced sympathetic response to a lab stressor (Fisher, Granger, & Newman, 2010).

Autonomic inflexibility has also been linked to panic disorder, and, thus, the physiological profile of GAD overlaps with other disorders (Hoehn-Saric, Schlund, & Wong, 2004). Nonetheless, research suggests that the physiological profile of GAD is related to a physiological-inhibitory effect of worry, the primary feature of the disorder. Relative to neutral thinking or relaxation, worrying prior to exposure to a phobic image is associated with decreased heart rate response during that subsequent image (Borkovec & Hu, 1990; Borkovec et al., 1993). Moreover, compared to neutral thinking, experimentally induced worry is also associated with decreased vagal tone, heart rate, and heart rate variability among individuals with and without GAD (Thayer et al., 1996; Lyonfields et al., 1995). Worry is also associated with decreased heart rate response during subsequent anxiety-eliciting tasks (increased heart rate during exposure is a marker of emotional processing; Foa & Kozak, 1986) while increasing subjective distress (e.g., Borkovec & Hu, 1990).

Patterns of connectivity between the amygdala, the medial prefrontal cortices, and other associated areas suggest the engagement of a compensatory, cognitive control system among individuals with GAD (Etkin, Prater, Schatzberg, Menon, & Greicius, 2009). Moreover, individuals with GAD fail to use the pregenual anterior cingulate to dampen amygdala activity and regulate emotions during laboratory emotional conflict tasks (Etkin, Prater, Hoeft, Menon, & Schatzberg, 2010). Interestingly, the medial prefrontal and anterior cingulate regions are associated with worry both in individuals with GAD and in normal controls, but only individuals with GAD show persistent activation in these areas following experimental worry periods (Paulesu et al., 2010). GAD is also associated with increased brain activity in response to both neutral and worry-related verbal statements, and reductions in that increased activity correspond to reductions in anxiety during treatment with citalopram (Hoehn-Saric et al., 2004). Lastly, compared to individuals without GAD, those with GAD show increased gamma-band EEG activity in areas associated with negative emotion, as well as increased subjective negative emotion while worrying (Oathes et al., 2008). Moreover, both of these were attenuated following treatment for generalized anxiety disorder.

The amygdala has also been implicated in GAD, but the findings are not entirely clear. For example, individuals with GAD show increased activity in the amygdala in response to neutral and aversive pictures (relative to healthy controls; Nitschke et al., 2009). In response to fearful faces, however, individuals with GAD show decreased amygdala activity (relative to individuals with social anxiety disorder and healthy controls; Blair et al., 2008). Finally, the neurochemical underpinnings of GAD likely involve abnormalities in several neurotransmitters, including gamma-aminobutyric acid (GABA), which is thought to mediate anxiety; norepinephrine (NE), a mediator of the sympathetic nervous system; and serotonin (5-HT), a target of efficacious pharmacologic treatment of GAD (Sinha, Mohlman, & Gorman, 2004).

Unlike other phobias, the BII subtype of specific phobia involves a parasympathetic response to feared stimuli. This response is distinct from fear responses in other phobias in that there is decreased blood pressure and vasodilation that results in pooling of the blood in the extremities. Page (1994) has suggested that this subtype can be further split into two distinct disorders, one that involves blood reactions, a parasympathetic response, and feelings of nausea and disgust; and another that

has a similar physiological reaction to that of other specific phobias and is characterized by fear of pain associated with needles and injury.

SPECIFIC GENES

Research on specific genes that confer risk for panic disorder has led to conflicting findings (see Maron et al., 2008; Schmidt et al., 2000). Linkage and association studies have examined several candidate genes known to be involved in the development of the brain structures associated with fear and fear learning. One gene (COMT) involved in the inactivation of dopamine in the prefrontal cortex appears to be associated with panic disorder (see Meaney et al., 2008). Also implicated are specific alleles of the serotonin transporter (5HTT) gene, which appear to play an important role in fear learning (Risbrough & Geyer, 2008). For example, in individuals who are carriers of particular alleles of 5HTT, the nonspecific experience of childhood maltreatment may lead to high levels of anxiety sensitivity (Stein, Schork, & Gelernter, 2008), a risk factor for panic disorder (see Personality and Temperament: Anxiety Sensitivity). Fewer investigations examined specific genes that confer risk for social anxiety disorder and specific phobias. The development of new gene technologies is quite likely to facilitate the search for specific genes and to clarify the ways in which genetic risk is conferred. Although this work is in its early stages, research on specific genes and gene-environment interactions holds promise for elucidating the development of these conditions and for informing approaches to prevention.

Some studies have found associations between specific genes and GAD. For example, variation in the monoamine oxidase A (MAOA) serotonin transporter genes may confer increased risk for GAD. In one study, a polymorphism in the MAOA gene was associated with GAD but not with panic disorder or major depressive disorder, whereas a different MAOA polymorphism was associated with GAD, panic attacks, and possibly specific phobia and agoraphobia (Tadic et al., 2003). Similarly, a variant in the serotonin transporter linked polymorphic region (5-HTTLPR) is overrepresented among individuals with GAD compared to normal controls (You, Hu, Chen, & Zhang, 2005). However, another study failed to replicate this finding (Samochowiec et al., 2004). Overall, specific genetic polymorphisms may increase risk for GAD and anxiety-related traits (e.g., neuroticism and anxiety sensitivity).

PERSONALITY AND TEMPERAMENT

Anxiety Sensitivity Anxiety sensitivity is a dispositional trait that is characterized by a fear of autonomic arousal and the physical sensations associated with anxiety states (e.g., increased heart rate, dizziness, nausea, shortness of breath; Reiss & McNally, 1985; Reiss, Peterson, Gursky, & McNally, 1986). Anxiety sensitivity, sometimes called the fear of fear, is conceptualized as the key feature of panic disorder (McNally, 1990; Taylor, 1999). Several investigations have indicated that individuals with panic disorder evidence high levels of anxiety sensitivity (e.g., Rapee, Brown, Antony, & Barlow, 1992), and individuals with panic disorder seem to have higher levels of anxiety disorders than do individuals with other anxiety disorders (Taylor, Koch, & McNally, 1992). It is important to note, however, that anxiety sensitivity is not unique to panic disorder; it is also an important construct in PTSD (McNally, Luedke, Besyner,

Peterson, Bohm, & Lips, 1987), depression (Schmidt, Lerew, & Jackson, 1997), and other anxiety disorders (Taylor et al., 1992).

Anxiety sensitivity also seems to be especially elevated in agoraphobia (Reiss et al., 1986). In a meta-analysis examining anxiety sensitivity across diagnostic groups, Olatunji and Wolitzky-Taylor (2009) concluded that anxiety sensitivity is substantially higher among individuals with panic disorder, GAD, social anxiety disorder, and PTSD compared to nonclinical controls (see also Naragon-Gainey, 2010), and that this difference is greater among females compared to males. In terms of differences between anxiety disorders, they found that (a) panic disorder was associated with greater levels of anxiety sensitivity compared to all other anxiety disorders except for PTSD; (b) PTSD was associated with greater levels of anxiety sensitivity compared to GAD and social anxiety disorder; and (c) levels of anxiety sensitivity among the other anxiety disorders (and mood disorders) generally did not differ from one another.

Evidence for anxiety sensitivity as a risk factor for the development of panic attacks comes from work by Schmidt, Lerew, and Jackson (1997, 1999), who conducted a prospective longitudinal study of Air Force recruits before and after a stressful 5-week cadet training program. Anxiety sensitivity before cadet training predicted frequency of panic attacks during boot camp, even after controlling for previous panic symptoms and trait anxiety. Although more research is needed to better understand how anxiety sensitivity develops and how it contributes to the development of panic disorder, anxiety sensitivity does seem to uniquely predict panic attacks and related symptoms (Maller & Reiss, 1992; Schmidt et al., 1997, 1999) as well as the development of anxiety disorders (Calkins et al., 2009; Maller & Reiss, 1992).

Behavioral Inhibition and Shy Temperament Behavioral inhibition has been proposed as an enduring tendency to respond to unfamiliar events with anxiety (Kagan, Reznick, & Snidman, 1987), and thus has obvious conceptual similarities to both shyness and social anxiety. Behavioral inhibition during the first few years of life predicts inhibited behavior with peers later in childhood (Aksan & Kochanska, 2004) and social anxiety disorder in adolescence (Chronis-Tuscan et al., 2009; Hayward, Killen, Kraemer, & Taylor, 1998; Schwartz, Snidman, & Kagan, 1999) and adulthood (Kagan & Snidman, 1999).

The relative stability of socially inhibited behavior from the first years of life until adulthood is consistent with the view of social anxiety disorder as rooted in relatively unchangeable, biologically based behavioral tendencies (i.e., temperament). It is notable, however, that a substantial number of children classified as having behavioral inhibition do not go on to develop social anxiety disorder (Hayward et al., 1998; Kagan & Snidman, 1999; Schwartz et al., 1999; Wittchen, Stein, & Kessler, 1999). Studies of behavioral inhibition might also provide a means for understanding how parental variables contribute to the development of social anxiety disorder (Moehler et al., 2007) and how chronic inhibition in social behavior may develop through a dynamic interplay between child characteristics and parenting.

Behavioral Considerations

Classical Conditioning Drawing upon the observation that fears can be acquired through a repeated process of paired learning, early behaviorists proposed that

phobias are acquired through classical conditioning (Mowrer, 1947). An early and famous demonstration of this approach involves the story of Little Albert, a 4-year-old boy who was conditioned to fear white rabbits after only a few conditioning trials (Watson & Rayner, 1920). Following this line of reasoning, a single conditioning trial with a sufficiently severe unconditioned stimulus could result in learned fear. Although classical conditioning of fear represents one way that fear can be acquired, it does not account for the fact that most individuals with specific phobias have not experienced such events. Inconsistent with the classical conditioning model, many individuals with no prior experience with the feared object or situation meet the criteria for specific phobia, and many individuals with seemingly traumatic conditioning experiences do not develop phobias (Rachman, 1989). Nevertheless, the view of specific phobias as a learned association has persisted and is consistent with views of exposure therapy as extinction.

Conditioning has also been applied to understanding the development of panic disorder. These efforts have sometimes been criticized as tautological because panic and anxiety are considered to be responses that become conditioned, but the conditioned stimuli are interoceptive symptoms associated with panic and anxiety (e.g., McNally, 1990). Bouton, Mineka, and Barlow (2001), however, point out that the tautology is resolved because panic and anxiety are distinct: Panic becomes conditioned to the symptoms of anxiety. Panic attacks in the context of panic disorder can be viewed as a highly generalized fear response, one in which one interoceptive stimulus (e.g., accelerated heart rate) may be sufficient to trigger an acute fear reaction even in the absence of any specific external stimulus.

Operant Conditioning Mowrer (1947) proposed that whereas fear is acquired via classical conditioning, it is maintained via operant conditioning. Specifically, he posited that the avoidance and escape behaviors that accompany phobic fear are maintained through a process of negative reinforcement in that they remove or prevent negative affective states. This position has become very influential in treatment models for anxiety disorders, providing a compelling rationale for the reduction or elimination of avoidance and safety behaviors in panic disorder, social anxiety disorder, and specific phobias (e.g., Bennet-Levy et al., 2004). Escape and avoidance behaviors are thought to maintain fear either through their prevention of fear activation (which is theorized to be a necessary precursor to habituation; Foa & Kozak, 1986) or through their prevention of disconfirmation of erroneous threat beliefs. In addition to escape from and avoidance of feared situations, subtle in-situation avoidance behaviors (also known as safety behaviors) have been identified as an important feature of these disorders (Helbig-Lang & Petermann, 2010). Operant behaviors are widely recognized as involved in the maintenance of anxiety disorders, but they are not usually seen as playing a substantial role in the early development of panic disorder, social anxiety disorder, or specific phobia.

Current theoretical conceptualizations of GAD posit that worry is in itself a type of avoidant response. Worry is predominantly a verbal-linguistic (as opposed to imagery-based) activity (Borkovec & Inz, 1990), and this predominance of verbal activity inhibits the somatic reactivity (Vrana, Cuthbert, & Lang, 1986) that is necessary for emotional processing of fear cues (Foa & Kozak, 1986). Although this inhibition of somatic activation reduces undesired distress in the short term, it prevents the

emotional processing of fear that is theoretically necessary for successful habituation and extinction to eventually take place (Foa & Kozak, 1986). The avoidance theory of worry (Borkovec, Alcaine, & Behar, 2004) thus argues that worry is an ineffective cognitive strategy that is maladaptively used to reduce threat that exists in the form of somatic, physiological fear.

Vicarious Conditioning In addition to classical conditioning, vicarious conditioning (sometimes called observational learning or learning by modeling) is now widely recognized as a means for developing a learned association, functionally equivalent to learning by classical conditioning. Acquisition of fear by vicarious conditioning is well-illustrated in a study by Cook and Mineka (1990). In that study, lab-reared monkeys who had never seen a snake were shown a videotape of wild-reared monkeys displaying fear of live and toy snakes. This vicarious conditioning experience was sufficient for the lab-reared monkeys to acquire a fear of snakes. Such processes are widely accepted to be relevant to human learning processes (Mineka & Zinbarg, 2006).

Vicarious conditioning may interact with temperament to predict the development of social anxiety disorder (Rapee & Spence, 2004). For example, de Rosnay, Cooper, Tsigaras, and Murray (2006) trained mothers to act in shy and nonshy manners with strangers. Their 12- to 14 month-old infants acted shyly in subsequent encounters with strangers following shy modeling (demonstrating vicarious learning), and this effect was particularly pronounced for those infants with an inhibited temperament.

Informational Acquisition Rachman (1977) suggested that phobias might be acquired in three ways: (1) classical conditioning, (2) vicarious conditioning, and (3) informational acquisition. Information acquisition involves the development of a fear as a result of receiving information, such as from a parent or doctor. Both vicarious and informational learning has also been documented for social anxiety disorder (Mulkins & Bögels, 1999). For example, Barrett, Rapee, Dadds, and Ryan (1996) found that when presented with threatening scenarios, children with anxiety disorders and their parents independently chose avoidant responses and that children's selection of avoidant responses increased after they interacted with their parents; such a pattern was not apparent among aggressive children. This familial enhancement of avoidant responding in children with anxiety disorders is consistent with informational acquisition. The three-pathways model proposed by Rachman (1977) has also been applied to understand the retrospective accounts of the onset of many types of specific phobias (King, Eleonora, & Ollendick, 1998).

Preparedness Theory One observation that challenges the behavioral view of phobias as learned associations is that common fears are not randomly distributed but are more frequently associated with stimuli that are objectively evolutionarily dangerous. To account for this observation, Seligman (1971) proposed the "preparedness theory," which posits that during the Paleolithic period of the evolution of the human species, survival and reproductive fitness were increased by fear and avoidance of objects and situations that were dangerous. Drawing upon preparedness theory, Mineka and Öhman (2001, 2002) proposed that humans are prepared to fear stimuli that are relevant to survival because we have evolved a module for fear learning that is

encapsulated and relatively independent of cognitive processing. This view proposes that fears of survival-relevant stimuli are relatively automatic and involve central brain regions. There is evidence for several aspects of this model (see Mineka & Öhman, 2001; Mineka & Zinbarg, 2006), including evidence of slower extinction to survival-relevant stimuli and limited penetrability to conscious cognitive control for fear of stimuli that are relevant to survival (Öhman & Soares, 1998).

Work by Cook and Mineka (1990, 1991, discussed earlier) illustrates preparedness to acquire fear of stimuli relevant to survival. Although lab-reared monkeys who had never seen a snake quickly acquired fear when presented with a videotape model, illustrating vicarious learning, no such learning took place when they were presented with a videotape model of a monkey displaying fear of stimuli that are irrelevant to survival, such as flowers and toy rabbits. Also, this preferential conditioning did not occur with learning of other responses (e.g., appetitive). Although such enhanced fear conditioning to evolutionarily dangerous stimuli has been displayed in monkeys, applicability of preferential conditioning in humans is somewhat less well-established (see Mineka & Zinbarg, 2006).

Another observation that is consistent with preparedness theory is the distribution of age of onset as a function of different types of specific phobia (Öst, 1987). Animal phobias tend to develop early (mean age of onset of 7 years of age), during an age when animals present the greatest objective threat. In contrast, claustrophobia tends to develop much later (mean age of onset of 20 years of age), during an age when taking refuge in an enclosed hiding place may be less advantageous.

Related to preparedness theory, an evolutionary view of blood reactions has also been proposed (Thyer, Himle, & Curtis, 1985). Fainting appears to be an adaptive response to injury, because decreased blood pressure and raising the wound site relative to the heart reduces and slows blood loss. The high heritability of blood reactions might help explain the higher and relatively more specific heritability of the BII subtype of specific phobia (see Merckelbach & de Jong, 1997).

Disgust has been implicated as a distinct emotional state that is involved in many anxiety disorders (Woody & Teachman, 2000). For example, animal phobias can be differentiated into those that involve contamination threat and disgust reactions (e.g., fear of rats) and those that involve predators and do not include disgust reactions (e.g., fear of dogs; Matchett & Davey, 1991). Disgust also appears to be relevant to other specific phobias (e.g., BII phobias), to obsessive-compulsive washers, and perhaps to social anxiety disorder in the form of self-disgust (Amir, Najmi, Bomyea, & Burns, 2010). The role of disgust in these anxiety disorders appears to reflect an avoidance of disease that is also evolutionarily advantageous (Matchett & Davey, 1991; Woody & Teachman, 2000).

COGNITIVE CONSIDERATIONS

Cognitive biases have often been noted in individuals diagnosed with panic disorder, GAD, social anxiety disorder, and specific phobias. These phenomena are usually described using an information-processing framework (Lang, 1979) for understanding pathological fear (Foa & Kozak, 1986; Rachman, 1980). Studies of these biases can be divided into those that focus on content (e.g., beliefs, expectancies, appraisals) and those that focus on process (e.g., attention, interpretation, memory). A key task in

evaluating cognitive approaches to understanding the etiology of these disorders is to identify which biases play a causal role and which are simply features or by-products of the disorders.

Situation-Specific Cognitions and Related Variables Approaches to understanding cognitive biases can be further divided into those that emphasize relatively enduring individual difference factors and situation-specific cognitions. Individual difference factors include anxiety sensitivity, which can be viewed as a tendency to engage in the situation-specific cognitions that cause panic attacks in the context of panic disorder (McNally, 1990). In addition, individual difference factors include core beliefs, which can be viewed as the latent variables that interact with situational variables to produce the automatic cognitions that are the proximal determinants of fear, anxiety, and avoidance behavior (Beck & Emery, 2005). The individual difference variable of fear of negative evaluation (Leary, 1983b), which can be viewed as the tendency to overestimate the likelihood and importance of being negatively evaluated when in a social situation, has become the axiomatic dimension associated with social anxiety disorder.

Regarding situation-specific cognitions, panic disorder, GAD, social anxiety disorder, and specific phobias have been characterized by overestimations of fear and danger. Evolutionarily, underestimation of fear and danger could be very costly to individuals, whereas overestimation of fear and danger were advantageous. Examining situation-specific cognitions under a variety of names (including expectancies, concerns, automatic thoughts, catastrophic thoughts, and catastrophic misinterpretations), researchers have generally found that situation-specific cognitions are predictors of fear, anxiety, and avoidance behavior. For example, expectancies appear to be proximal cognitive determinants of fear and fear behavior (e.g., Valentiner, Telch, Petruzzi, & Bolte, 1996). The types of expectancies and concerns that are most important are believed to vary across different types of fear stimuli: Acrophobia is believed to involve expectances of falling (Menzies & Clarke, 1995), whereas claustrophobia is believed to involve expectancies of suffocation and entrapment (Radomsky, Rachman, Thordarson, McIsaac, & Teachman, 2001; Valentiner et al., 1996). Panic attacks in the context of panic disorder are believed to involve misinterpretation of bodily sensations, resulting in catastrophic thoughts related to heart dysfunction, suffocation, and mental control (Cox, 1996).

Another situation-specific cognitive variable that has been implicated for these disorders is self-efficacy, which is conceptualized as a higher-order cognitive process that incorporates lower-order cognitions, including estimates of one's coping capacities in addition to expectancies of anxiety and expectancies of danger (Bandura & Adams, 1977). Although there are methodological concerns about how the self-efficacy construct is typically operationalized, there is some evidence for self-efficacy as a unique predictor of fear and fear behavior for panic disorder (Cho, Smits, Powers, & Telch, 2007) and specific phobias (Valentiner et al., 1996). Furthermore, individuals with GAD overestimate the likelihood of negative future events and underestimate their ability to cope with negative outcomes should they occur (Borkovec, Hazlett-Stevens, & Diaz, 1999).

Situation-specific cognitions and individual differences in the tendency to engage in situation-specific cognitions have proven to be useful to understanding panic

disorder, GAD, social anxiety disorder, and specific phobias. These content variables predict changes in functioning over time and during treatment (e.g., Hoffman, 2004; Wilson & Rapee, 2005), and manipulations that target these cognitions appear to improve the ability of behavioral treatment techniques in reducing symptoms of panic disorder (e.g., Murphy, Michelson, Marchione, Marchione, & Testa, 1998), social anxiety disorder (e.g., Kim, 2005), GAD (Borkovec, Newman, Pincus, & Lytle, 2002), and specific phobias (e.g., Kamphuis & Telch, 2000).

Attentional Biases and Related Cognitive Processes Regarding studies of cognitive biases that focus on process, a good deal of research has examined attentional processes (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007). Anxiety has been found to be associated with biases in various attentional processes, namely orienting, engagement, and disengagement (see Ouimet, Gawronski, & Dozois, 2009). In addition, attentional biases have been found, using a variety of tasks, to occur in all anxiety disorders (see Cisler & Koster, 2010), including panic disorder (e.g., Buckley, Blanchard, & Hickling, 2002), social anxiety disorder (e.g., Amir, Elias, Klumpp, & Przeworski, 2003), GAD (e.g., Bradley, Mogg, White, Groom, & de Bono, 1999) and specific phobias (e.g., Watts, McKenna, Sharrock, & Trezise, 1986).

Some researchers (Bögels & Mansell, 2004), however, have viewed the evidence for attentional biases in social anxiety disorder as somewhat mixed. In addition, there may be differences in attentional biases as a function of social anxiety disorder subtype. McNeil et al. (1995) found evidence for cognitive interference (using the emotional Stoop task) on general social words and speech-specific words for the generalized subtypes of social anxiety disorder, but only for speech-specific words for the nongeneralized subtype.

The overall picture that emerges is one in which attentional biases are strongly implicated in anxiety disorders, including panic disorder, GAD, social anxiety disorder, and specific phobias (Bar-Haim et al., 2007; Ouimet et al., 2009). The attentional bias appears to be content-specific, with, for example, spider phobics showing attentional biases to spiders (Watts et al., 1986). The pattern that emerges involves an attentional bias toward threatening stimuli evident early in the attentional process, followed by difficulty disengaging from threatening stimuli, and then later avoidance of threatening stimuli (Cisler & Koster, 2010). In addition, retraining of attentional bias appears to reduce fear and avoidance (Amir, Weber, Beard, Bomyea, & Taylor, 2008; Bar-Haim, 2010). This emerging approach is attractive because relatively brief interventions that modify attention biases may undermine the development or maintenance of anxiety conditions. Thus, attention bias modification might be delivered as an adjunct to enhance exposure-based treatments or as stand-alone approaches for prevention in high-risk populations (Bar-Haim, 2010).

A variety of other cognitive process variables have been proposed as being involved in the development and maintenance of these disorders. For example, interpretation biases have been demonstrated for panic disorder (Westling & Öst, 1995) and social anxiety disorder (Amir, Foa, & Coles, 1998). Implicit memory bias has been found in panic disorder (Amir, McNally, Riemann, & Clements, 1996). Evidence for a memory bias in social anxiety disorder is weak, although some authors suggest that such a bias might only be evident in the context of an imminent social threat (Hirsch & Clark, 2004).

One cognitive process that has been shown to play a role in social anxiety disorder is postevent processing (cf. rumination), repetitive self-focused thought in which one's social performance is reconstructed and distorted to be consistent with the pathological beliefs underlying social anxiety (see Brozovich & Heimberg, 2008). Similar processes may be involved in the development of panic disorder and specific phobias, as Davey and Matchett (1994) have demonstrated that mental rehearsal of a conditioning trial can enhance conditioned fears.

Self-Focused Attention A cognitive process variable that appears to be particularly relevant to social anxiety is that of self-focused attention, or the tendency for socially anxious individuals to attend to internal stimuli rather than external, social stimuli. These internal stimuli are believed to include both interoceptive sensations (e.g., racing heart) and negative images of the self and behavior. Consistent with the social anxiety disorder model proposed by Clark and Wells (1995; see also Clark, 2001), self-focused attention when in social situations appears to be an important cognitive feature of the disorder, as well as an important factor in the maintenance of social anxiety (Bögels & Mansell, 2004), leading to an increased awareness of anxiety responses (Alden & Mellings, 2004) and a disruption of the realistic processing of the situation and other people's behaviors (Bögels & Lamers, 2002). Targeting self-focused attention appears to improve outcomes during exposure-based treatment for social anxiety disorder (Wells & Papageorgiou, 1998).

Culture, Socialization, and the Social Environment

Messages that parents give to their children about the meaning and importance of their interoceptive sensations, through parental reinforcement of illness behavior, may play a role in the development of panic attacks and panic disorder. A retrospective study by Stewart et al. (2001) provides evidence that childhood learning experiences with respect to arousing-reactive symptoms (e.g., racing heart, shortness of breath, etc.) but not arousing-nonreactive symptoms (e.g., colds, aches, rashes, etc.) contributed to the frequency and intensity of panic attacks. This effect appeared to be partially mediated by anxiety sensitivity.

Compared to control participants, individuals with GAD report a history of rejection and neglect from their mothers, along with more frequent role-reversed/enmeshed relationships (in which the child must take care of the mother), as well as current feelings of vulnerability toward their mothers (Cassidy, Lichtenstein-Phelps, Sibrava, Thomas, & Borkovec, 2009).

Social factors also appear to play an important role in the development and course of social anxiety disorder. For example, poorer social relationships have been observed in shy children (Gazelle & Ladd, 2003; Rubin, Wojslawowicz, Rose-Krasnor, Booth-LaForce, & Burgess, 2006) and among children (Alden & Taylor, 2004) and adults (Lampe, Slade, Issakidis, & Andrews, 2003; Whisman, Sheldon, & Goering, 2000) diagnosed with social anxiety disorder. The social deficits associated with social anxiety disorder and shyness include peer neglect (Gazelle & Ladd, 2003), fewer positive responses (Spence, Donovan, & Brechman-Toussaint, 2000), and peer victimization (Hawker & Boulton, 2000; La Greca & Harrison, 2005; McCabe, Antony, Summerfeldt, Liss, & Swinson, 2003; Siegel, La Greca, & Harrison, 2009; Storch &

Masia-Warner, 2004). Social deficits, such as peer rejection, appear to be mediated by poor social skills (Greco & Morris, 2005), although individuals with social anxiety disorder do not always show poor social skills (e.g., Beidel, Turner, & Jacob, 1989). It should also be noted that peer victimization may be both a cause (Bond, Carlin, Thomas, Rubin, & Patton, 2001) and a consequence of social anxiety, as social anxiety predicts subsequent victimization (Siegel et al., 2009).

In a study by Daniels and Plomin (1985), mothers' sociability was significantly associated with the shyness of their adopted infants, and genetic influences were ruled out given that the infants in the study had been adopted. In addition, the effect was still evident after controlling for maternal shyness, largely ruling out modeling or social learning interpretations.

Culture may also play a role in the expression of panic disorder and other anxiety conditions. *Ataque de nervios* is an acute set of symptoms and behaviors that shares some similarities with a panic attack, although typically experienced in response to a stressful family event and incorporating a volitional behavior component (APA, 2000). It is not clear whether this and other culture-specific anxiety conditions represent an inapplicability of our nosological system to Latin American and Caribbean cultures, a culture-specific expression of known anxiety disorders such as panic disorder, or something else (Guarnaccia, Lewis-Fernández, & Marano, 2003). In addition, the definitional requirement that panic attacks reach a peak within 10 minutes and the duration of panic attacks may vary as a function of culture (Lewis-Fernández et al., 2010).

Cultural factors likely play a role in the development of social anxiety as well. For example, culture-specific norms appear to impact the acceptability of socially inhibited behavior and affect the expression of social anxiety (Heinrichs et al., 2006). In addition, culture likely affects the expression of social anxiety. As discussed earlier, Taijin Kyofusho has been viewed as a culturally bound syndrome thought to appear only in Japan and Korea (APA, 2000; cf. anthropophobia, WHO, 1992). More information about the likely role of cultural attitudes, beliefs, norms, and practices on the development and expression of social anxiety is needed.

Life Events

Stress, including life events and chronic conditions such as maltreatment during childhood, appears to increase risk for a variety of mental disorders, including anxiety disorders (Allen, Rapee, & Sandberg, 2008; Kessler, Davis, & Kendler, 1997; Phillips, Hammen, Brennan, Najman, & Bor, 2005). Past traumatic events may contribute to feelings of anxious apprehension and the perception that the world is a dangerous place (Borkovec, Alcaine, & Behar, 2004). Stressful events also impact the maintenance and course of panic disorder (Craske, Rapee, & Barlow, 1988), agoraphobia (Rachman, 1984), GAD (Roemer, Molina, Litz, & Borkovec, 1997), social anxiety disorder (Mineka & Zinbarg, 1996), and specific phobias (Craske, 1991).

Individuals with GAD are more likely to have experienced the death of a parent before the age of 16 compared to individuals with panic disorder and controls (Torgersen, 1986). Furthermore, life events that contribute to GAD may differ from those that contribute to depression; events characterized by loss and danger may convey specific vulnerability to noncomorbid GAD, whereas loss and humiliation may be more specific to major depressive disorder (Kendler, Hettema, Butera,

Gardner, & Prescott, 2003). A 32-year longitudinal study found several risk factors associated with GAD but not with major depressive disorder, including low socioeconomic status, maternal internalizing symptoms, maltreatment, inhibited temperament, internalizing and conduct problems, and negative emotionality (Moffitt et al., 2007).

Consistent with a conditioning model, individuals with social anxiety disorder retrospectively report greater incidence of traumatic social events than do healthy controls, and this greater incidence appears to be higher for those with the non-generalized subtype compared to the generalized subtype (Stemberger, Turner, Beidel, & Calhoun, 1995).

Early studies suggest that onset of panic disorder, GAD, social anxiety disorder, and specific phobias are sometimes triggered by the occurrence of a stressful life event. This phenomenon may reflect fear inflation (Mineka & Zinbarg, 1996; Rescorla, 1974), which takes place when a person or animal undergoes conditioning of mild fear, such as through classical conditioning, and then experiences an intense, unpaired exposure to the unconditioned stimulus, so that the previously mild fear increases in strength. More recent evidence has found no greater rates of stressful life events prior to anxiety disorder onset than at other times (Calkins et al., 2009).

The phenomenon of latent inhibition, in which prior benign (nonfearful) exposure to a stimulus inhibits fear acquisition, is a well-established finding in the animal literature that informs how we think about fear learning in humans (see Mineka & Zinbarg, 2006). Prior exposure also reduces generalization of fear (Vervliet, Kindt, Vansteenwegen, & Hermans, 2010), an observation that may be especially relevant to the development of panic disorder, which is sometimes viewed as involving highly generalized fear responses (Gorman et al., 2001). Related to these ideas, positive control experiences early in life appear to provide protection against fear conditioning and the development of anxiety disorders (see Chorpita & Barlow, 1998).

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CHAPTER 9

Obsessive-Compulsive and Related Disorders

SANDRA M. NEER and KATIE A. RAGSDALE

Obsessive-compulsive and related disorders is a new category in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*; American Psychiatric Association [APA], 2013) and includes obsessive-compulsive disorder (OCD), body dysmorphic disorder (BDD), hoarding disorder (HD), trichotillomania (TTM), and excoriation (skin-picking) disorder (ED). The new *DSM-5* category includes disorders previously categorized elsewhere within the *DSM-IV-TR* (APA, 2000) (e.g., anxiety disorders [OCD], somatoform disorders [BDD], and impulse-control disorders not elsewhere classified [TTM]), as well as two new diagnoses (HD and ED). The disorders were reclassified within this new category to reflect their diagnostic and clinical relatedness (APA, 2013).

Diagnostically, OCD is characterized by obsessions and/or compulsions that consume more than 1 hour per day or cause clinically significant distress or impairment (APA, 2013). Obsessions include recurrent and persistent thoughts, urges, or images (e.g., thoughts of contamination or urges to kill someone) of an intrusive or unwanted nature, which individuals attempt to suppress, ignore, or neutralize (e.g., by performing a compulsion). Compulsions are repetitive behaviors or mental acts (e.g., counting or washing) individuals engage in to prevent or reduce anxiety or distress. Compulsions do not need to be logically connected to the obsessions they are attempting to neutralize, although they often are.

BDD is defined by a preoccupation with perceived physical defects or flaws that, at some point during the course of the disorder, result in repetitive behaviors (e.g., mirror checking) or mental acts (e.g., appearance comparisons) (APA, 2013). Preoccupation can occur with any part of the body (e.g., hair, face shape, or nose) but is most commonly associated with the skin (e.g., wrinkles or scars). Although the perceived defects or flaws cause clinically significant distress or impairment to the individual, they appear minor or unrecognizable to others. Individuals who are preoccupied with body build, believing that the body is too small or insufficiently muscular, would meet criteria for the specification of BDD with muscle dysmorphia. Additionally, clinicians can specify whether an individual's level of insight is good, fair, poor, or absent. In a

case where an individual is completely convinced of their defect, absent insight/delusional beliefs may be specified.

HD, a new diagnosis of the *DSM-5*, reflects persistent difficulty parting with possessions to the point that it causes clinically significant distress or impairment (APA, 2013). Difficulty discarding an item is unrelated to the item's actual value; rather, it is related to both the distress associated with discarding the item and a perceived need to save it. As a result, accumulation of possessions causes congestion and clutter in living areas, which substantially compromises their intended uses. In addition, individuals who excessively acquire additional possessions which are not needed or for which there is no room would meet criteria for the specification of HD with excessive acquisition.

TTM (hair-pulling disorder) is defined by recurrent hair pulling that results in hair loss. Although hair pulling typically results in visible hair loss, individuals who widely pull hair from various body regions may not evidence this clinical marker (APA, 2013). The scalp, eyelids, and eyebrows are the most common sites; however, hair pulling may occur at any region of the body where hair grows. In addition to hair pulling, individuals suffering from TTM repeatedly attempt to decrease or stop hair pulling, and endorse significant associated distress or impairment.

ED (skin picking), also a new disorder to the *DSM-5*, is characterized by recurrent skin picking which results in skin lesions (APA, 2013). Skin picking commonly occurs on the face, arms, and hands; however, individuals may pick various body regions (APA, 2013). Although individuals typically use fingernails to pick, other objects (e.g., tweezers) and techniques (e.g., squeezing or rubbing) may be used. Individuals may pick at a variety of sites including healthy skin, scabs, or skin irregularities, and repeatedly attempt to decrease or stop skin picking. As with all other psychiatric disorders, individuals must experience clinically significant distress or impairment to meet diagnostic criteria.

Clinical Features

OCD is a clinically heterogeneous disorder with various presentations of obsessions and/or compulsions. Although individuals do not need to endorse both obsessions and compulsions to meet diagnostic criteria (APA, 2013), 96% of outpatients with OCD report experiencing both, whereas 2% endorse predominant obsessions and 2% report predominant compulsions (Foa & Kozak, 1995). Among this large sample of individuals from the *DSM-IV* field trials, the most common obsession reported was contamination (37.8%), followed by fear of harming self or others (23.6%) and symmetry (10%). The most common compulsions reported were checking (28.2%) and cleaning/washing (26.6%). Other obsessions included somatic, religious, and sexual obsessions, whereas other compulsions included repeating, mental rituals, ordering, and counting.

A meta-analysis of factor analytic studies of OCD symptom categories revealed four factors, which explained nearly 80% of the variance in 17 studies of adults with OCD (Bloch, Landeros-Weisenberger, Rosario, Pittenger, & Leckman, 2008). The four factors included symmetry (symmetry obsessions and repeating, counting, and ordering compulsions), cleaning (contamination obsessions and cleaning compulsions), forbidden thoughts (aggressive, religious, and sexual obsessions), and hoarding

(hoarding obsessions and compulsions). Often, obsessions and compulsions are functionally related (e.g., contamination fears accompanied by cleaning rituals or self-doubt and dread accompanied by repetitive checking; Turner & Beidel, 1988). For instance, strong associations exist between some similar obsessions and compulsions (e.g., contamination obsessions and cleaning compulsions), whereas others are less specific (e.g., checking compulsions are related to a variety of obsessions) (Bloch et al., 2008).

OCD is a debilitating disorder with significant functional impairment and reduced quality of life (Norberg, Calamari, Cohen, & Riemann, 2008). In fact, a recent review found that quality of life in OCD is significantly lower than quality of life in community controls and individuals with other psychiatric and medical disorders (Macy et al., 2013). Unfortunately, despite the associated impairment and distress, few individuals with the disorder initiate treatment (Levy, McLean, Yadin, & Foa, 2013).

Clinically, BDD is marked by preoccupation with physical appearance that results in repetitive behavioral or mental acts. On average, preoccupation is focused on five to seven areas of the body (Phillips, Menard, Fay, & Weisberg, 2005). Although the clinical presentation in men and women is more similar than different, implicated body regions differ significantly (Phillips, Menard, & Fay, 2006). Men are more likely to be preoccupied with body build, genitals, and hair thinning or balding, whereas women are more likely to be preoccupied with a wider variety of body areas (i.e., skin, stomach, weight, breasts, buttocks, thighs, legs, hips, toes, and excessive body or facial hair). Repetitive or safety behaviors in response to body preoccupation may include comparison to others, camouflaging (i.e., using body posture or position, clothes, and makeup, among others, to hide the perceived defect), mirror checking, grooming, reassurance seeking, dieting, and tanning (Phillips et al., 2005).

Individuals with BDD endorse high rates of both suicidal ideation and suicide attempts due to appearance concerns (Rief, Buhlmann, Wilhelm, Borkenhagen, & Brähler, 2006). For instance, in a sample of 200 individuals with BDD, 81.3% of treated subjects and 71.2% of untreated subjects endorsed suicidal ideation, and over a quarter of all subjects had attempted suicide (Phillips et al., 2005). Further, individuals with the disorder are more likely to be divorced, unmarried, unemployed, and have lower incomes than individuals without the disorder (Rief et al., 2006) and may be housebound, miss work and school, drop out of school, and receive disability (Phillips et al., 2005). Despite the associated distress and impairment, few individuals with BDD disclose their body image concerns to clinicians, most often due to feelings of embarrassment or fears of being negatively evaluated (Conroy et al., 2008). Instead, many individuals with the disorder receive nonpsychiatric treatment (i.e., dermatology and cosmetic surgery) (Phillips et al., 2005).

The typical clinical presentation of HD involves an individual who has significant difficulty parting with possessions and associated distress and impairment. Over two-thirds of individuals with the disorder may also exhibit excessive acquisition of items, which has been found to be a clinical predictor of distress and/or impairment (Timpano et al., 2011). Individuals with the disorder most frequently accumulate items through purchase (64.4%) and obtaining free things (53.4%); however, a subsample of those who engage in excessive acquisition may also steal (25.3%).

Clinically significant hoarding may lead to work impairment, eviction from the home, and/or removal of others from the home, and is a significant public health burden (Tolin, Frost, Steketee, Gray, & Fitch, 2008).

The hallmark symptom of TTM is clinically significant hair pulling. Individuals usually pull hair from multiple sites, most frequently being the scalp, followed by eyelashes, eyebrows, and pubic hair (Flessner, Woods, Franklin, Keuthen, & Piacentini, 2009). Although it is not necessary for diagnosis, many adults with the disorder report an urge, need, or drive to pull hair, as well as a sense of gratification or relief during or after pulling (Lochner et al., 2012). Most individuals pull out single hairs (68%); however, some may pull out clumps (5%), or a combination of single hairs and clumps (27%) (Christenson, MacKenzie, & Mitchell, 1991). Additionally, individuals may target specific types of hair based on thickness, texture, or color and may manipulate hair after it is pulled (e.g., suck on hairs or scrape off roots) (Walsh & McDougle, 2001). Finally, individuals with TTM may express associated negative affective states, including feeling unattractive (87%), secretiveness (83%), shame (75%), irritability (71%), low self-esteem (77%), and depressed mood (81%) (Stemberger, Thomas, Mansueto, & Carter, 2000).

ED describes clinically significant picking of the skin that results in skin lesions. An examination of 60 individuals with pathologic skin picking suggests that the disorder is time-consuming and associated with various complications (Odlaug & Grant, 2008). Results of this study also suggest that individuals often begin picking in response to triggers, such as feel (55%) or sight (26.7%) of the skin, boredom/downtime (25%), and stress (20%). The face and head (60%) are the most common sights for picking, followed by the legs and feet (33.3%), arms (30%), torso (23.3%), and hands and fingers (21.7%). Most individuals (68.8%) pick from multiple sites of the body, often switching areas in order for other sites to heal. In fact, 35% of this sample experienced infections requiring antibiotics as a result of skin picking.

DIAGNOSTIC CONSIDERATIONS

The National Comorbidity Survey Replication (NCS-R; Kessler et al., 2004) found that 90% of individuals with a lifetime diagnosis of OCD met criteria for an additional *DSM-IV* disorder (Ruscio, Stein, Chiu, & Kessler, 2010). The most common comorbid disorders were anxiety disorders (75.8%), followed by mood disorders (63.3%), impulse-control disorders (55.9%), and finally substance use disorders (38.6%). Within anxiety disorders, the highest comorbidity rates were found for lifetime social phobia (43.5%), specific phobia (42.7%), and separation anxiety disorder (37.1%); whereas major depressive disorder (40.7%) was the most frequent comorbid mood disorder. Another study that examined a wider variety of *DSM-IV* disorders also found high rates of lifetime anxiety and depression comorbidity, as well as high rates of lifetime comorbid obsessive-compulsive personality disorder (24.7%) in individuals with OCD (Pinto, Mancebo, Eisen, Pagano, & Rasmussen, 2006).

In a sample of 200 individuals with BDD, lifetime comorbidity was compared in treated and untreated individuals (Phillips et al., 2005). Comorbidity rates were highest for mood (88.1% in treated individuals and 75.8% in untreated individuals), anxiety (73.1% and 62.1%, respectively), substance use (50.0% and 43.9%, respectively), and personality disorders (47.9% and 39%, respectively). The highest rate of

comorbidity for both samples was major depression (75.4% and 72.7%, respectively); however, rates were relatively high for social phobia (40.3% and 34.8%, respectively) and avoidant personality disorder (26.9% and 22.0%, respectively), which are likely related to appearance concerns associated with BDD.

Literature on the comorbidity rates of HD is sparse, likely due to its introduction as a stand-alone disorder in the *DSM-5*. However, one recent study did examine current comorbidity of HD (defined by the then-proposed *DSM-5* criteria) in 217 individuals with the diagnosis (Frost, Steketee, & Tolin, 2011). Major depression was the most common comorbid mood disorder (50.7%); however, comorbidity rates were also high for attention-deficit/hyperactivity disorder inattentive type (27.8%), generalized anxiety disorder (24.4%), social phobia (23.5%), and OCD (18%).

Similarly, research examining comorbidities of TTM is limited. A recent review suggests mood, anxiety, and substance use disorders are the most commonly identified comorbidities (Duke, Keeley, Geffken, & Storch, 2010). In addition, TTM is related to skin-picking disorder (Snorrason, Belleau, Woods, 2012), which is discussed in more detail next.

Although no literature exists at this time that examines comorbidities of *DSM-5* ED, earlier studies examining pathologic skin picking do exist. In one study, comorbidity was examined in a small sample ($n = 60$) of individuals who engaged in pathologic skin picking, defined similarly to the *DSM-5* criteria (with the exception of inclusion of preoccupation, tension, and relief criteria). Results found that 38.3% of individuals met current criteria for an additional *DSM-IV* disorder, whereas 56.7% met lifetime criteria for another disorder (Odlaug & Grant, 2008). Specifically, 36.7% of individuals met current criteria for TTM (with a similar rate for lifetime diagnosis [38.3%]), 15.0% met criteria for current OCD (16.7% for lifetime), and 15.0% met current criteria for major depressive disorder (31.7% for lifetime). Indeed, the comorbidity of TTM and skin-picking disorder appears to be high, with an average of 20.8% of TTM outpatient samples endorsing skin picking, and an average of 15.5% of skin-picking disorder outpatient samples endorsing TTM, indicating relatedness between the two disorders (Snorrason et al., 2012).

Epidemiology

Due to the recent advent of the *DSM-5,* current epidemiological studies reflect diagnoses largely based on *DSM-IV-TR* criteria. Diagnostic changes introduced in the *DSM-5,* as well as inclusion of new disorders, will likely generate new research that may elucidate changes in prevalence rates reflective of new diagnostic criteria. Thus, epidemiological data reflected here are based on *DSM-IV-TR* criteria and in samples of U.S. adults, unless otherwise noted.

Although over one-fourth of individuals report experiencing obsessions or compulsions at some point in their lives, meeting diagnostic criteria for OCD occurs in a much smaller percentage of individuals (Ruscio et al., 2010). Specifically, the 12-month prevalence rate of OCD is 1.2% and the lifetime prevalence rate is 2.3%. As a result, OCD is a relatively rare disorder.

In a nationally representative study, the point prevalence of BDD was 2.4% (Koran, Abujaoude, Large, & Serpe, 2008); however, rates vary widely depending on the setting. In one study, 1.8% of outpatient adults met criteria for BDD (van der Meer

et al., 2012), whereas rates in inpatient samples range from 13.1% to 16% (Conroy et al., 2008; Grant, Kim, & Crow, 2001).

Using the *DSM-IV* hoarding criterion of obsessive-compulsive personality disorder (i.e., being "unable to discard worn-out or worthless objects even when they have no sentimental value") (APA, 1994), the weighted community prevalence was 5.3% (Samuels et al., 2008). Similarly, in a large German community sample, 5.8% of individuals endorsed current hoarding according to (then proposed) *DSM-V* criteria (Timpano et al., 2011).

In a community sample, 0.6% of individuals met *DSM-IV-TR* criteria for TTM; however, the prevalence increased to 1.2% when the prior diagnostic criteria of building tension or release were ignored (Duke, Bodzin, Tavares, Geffken, & Storch, 2009), suggesting that the *DSM-5* criteria may be less restrictive and produce larger prevalence rates. Among a psychiatric inpatient sample, the point prevalence of TTM was 3.4% and the lifetime prevalence was 4.4% (Grant, Levine, Kim, & Potenza, 2005). Interestingly, a similar rate of TTM (3.9%) was found for a sample of college students; however, the latter rate was based on a modified self-report measure of the clinical interview administered to the inpatient sample (Odlaug & Grant, 2010).

Although ED was not an official diagnosis within the *DSM-IV-TR* (APA, 2000), prevalence rates based on various diagnostic criteria do exist. For instance, in non-clinical community samples, 1.4% to 5.4% of individuals endorsed clinically significant skin picking with associated distress or impairment (Hayes, Storch, & Berlanga, 2009). In a recent study examining prevalence based on (then proposed) *DSM-5* criteria, 4.2% of college students met diagnostic criteria for ED (Odlaug et al., 2013).

Psychological and Biological Assessment

Various clinician-administered measures for the assessment of OCD exist. For instance, the Anxiety Disorders Interview Schedule for *DSM-IV* (ADIS-IV; Brown, DiNardo, & Barlow, 1994) and the Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders (SCID-CV; First, Spitzer, Gibbon, & Williams, 1996) are semistructured diagnostic interviews that assess for OCD and other disorders. Additionally, the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS; Goodman et al., 1989a; Goodman et al., 1989b) is considered the "gold standard" for assessing OCD symptom severity and now includes a revised second edition (Y-BOCS-II; Storch, Rasmussen, et al., 2010). The Y-BOCS-II is a semi-structured, clinician-administered measure that assesses for the frequency and severity of OCD symptoms over the past week, with good to excellent psychometric properties (Storch, Larson, et al., 2010; Storch, Rasmussen, et al., 2010).

Although OCD is typically assessed using semi-structured clinical interviews, various self-report measures with established reliability and validity exist, including the Y-BOCS-Self Report (Baer, Brown-Beasley, Sorce, & Henriques, 1993; Steketee, Frost, & Bogart, 1996) and Obsessive-Compulsive Inventory (OCI; Foa et al., 2002). Finally, behavioral avoidance tests (BATs), or observational tasks in which individuals are exposed to feared stimuli while rating their distress, have recently been used to assess OCD (Grabill et al., 2008). Specifically, BATs are often administered before treatment to assess the severity of avoidance and distress, and after treatment to assess functional change. Although BATs provide additional clinical information, they are

generally considered an adjunct to traditional clinical interviewing, providing particularly helpful information for development of exposure hierarchies. For recent comprehensive reviews of assessment measures for OCD, see Benito and Storch (2011) and Grabill et al. (2008).

Although the SCID-CV (First et al., 1996) screens for BDD, more thorough assessments are needed for diagnosis. For example, the BDD Examination (BDDE; Rosen & Reiter, 1996), a 34-item semi-structured clinical interview, is designed specifically to diagnosis BDD. The BDDE has acceptable reliability and validity, and measures not only the various aspects of preoccupation, but also the level of conviction the individual holds regarding the perceived defect (Cororve & Gleaves, 2001). In addition, the Y-BOCS (Goodman et al., 1989a; Goodman et al., 1989b) was modified for the assessment of BDD (Y-BOCS-BDD; Phillips et al., 1997); however, the measure has been criticized for a narrow focus of obsessive compulsive type symptomatology (Rosen & Reiter, 1996).

The majority of current measures that assess for hoarding are based on *DSM-IV-TR* criteria (APA, 2000), which conceptualized hoarding as a symptom of OCD or a criterion of obsessive-compulsive personality disorder (Frost, Steketee, & Tolin, 2012). Although hoarding subscales exist on some measures of OCD, more recent measures designed specifically for hoarding have been created and may more accurately assess the diagnostic criteria of the disorder. For instance, the Hoarding Rating Scale-Interview (HRS-I; Tolin, Frost, & Steketee, 2010) is a five-item semi-structured clinical interview used to assess compulsive hoarding and related impairment and distress. The HRS-I exhibits excellent reliability, is sensitive to treatment changes, and can distinguish individuals with hoarding from both OCD patients without hoarding and community controls (Tolin et al., 2010). Additionally, the Saving Inventory–Revised (SI-R; Frost, Steketee, & Grisham, 2004) is a 23-item self-report measure that assesses for clutter, difficulty discarding, and excessive acquisition, which exhibits appropriate reliability and validity. For more comprehensive reviews of assessment of hoarding, see Frost et al. (2012) and Frost and Hristova (2011).

Although no gold standard assessment for TTM exists, there are some measures designed to assess for the disorder (Duke et al., 2010). Measures with acceptable psychometric properties include the Massachusetts General Hospital Hairpulling Scale (MGH-HPS; Keuthen et al., 1995; O'Sullivan et al., 1995), a seven-item self-report scale, and the Milwaukee Inventory for Subtypes of Trichotillomania-Adult Version (MIST-A; Flessner, Woods, Franklin, Cashin, & Keuthen, 2008), a 15-item scale that provides two distinct scale scores (i.e., automatic pulling and focused pulling scores).

There does not appear to be an assessment measure yet developed for the DSM-5 diagnosis of ED; however, some measures do assess for factors related to earlier conceptualizations of skin picking. For instance, the Skin Picking Scale (SPS; Keuthen et al., 2001) is a six-item self-report measure modeled after the original Y-BOCS (Goodman et al., 1989a; Goodman et al., 1989b); however, the measure only assesses for severity of skin picking. Further, similar to the MIST-A (Flessner et al., 2008), the Milwaukee Inventory for the Dimensions of Adult Skin Picking (MIDAS; Walther, Flessner, Conelea, & Woods, 2009) is a reliable and valid assessment of automatic and focused skin picking for individuals who engage in the behavior. Even so, assessment of ED is currently lacking due to the recent advent of the disorder in the latest *DSM-5*.

Clinical interviews or self-report measures that assess for the presence of *DSM-5* criteria are of particular need.

ETIOLOGICAL CONSIDERATIONS

BEHAVIORAL AND MOLECULAR GENETICS

OCD has a complex etiology involving both genetic and environmental factors. Evidence from family, twin, and segregation studies shows that heredity plays a major role in the etiology of OCD. In a meta-analytic study, Hettema, Neale, and Kendler (2001) found an average prevalence rate of 8.2% for first-degree relatives of OCD probands compared to 2% in comparison relatives, suggesting heritability. Twin studies of OCD patients also support the presence of significant genetic influence, with estimates of 45% to 65% in children, and 27% to 47% in adults (Jonnal, Gardner, Prescott, & Kendler, 2000). In a large twin study examining heritability of dimensions of OCD, including rumination, contamination, and checking, genetic factors accounted for 36% of the variance for an overall factor of OCD symptoms (van Groothest, Boomsma, Hettema, & Kendler, 2008). The remaining 64% was explained by environmental factors. Only the contamination dimension appeared to be influenced by specific genes and to be an independent dimension.

In another study of OCD symptom dimensions, five major symptom dimensions (checking, hoarding, obsessing, ordering, and washing) were analyzed in a sample of female twins (Iervolino, Rijsdijk, Cherkas, Fullana, & Mataix-Cols, 2011). The authors concluded that no single underlying factor could explain the heterogeneity of OCD. However, the majority of the genetic variance was due to shared genetic factors (62.5%–100%), whereas the nonshared environmental variance was due to dimension-specific factors (Iervolino et al., 2011). In this study, the hoarding dimension had the lowest loading on the common factor and was more influenced by specific genetic effects (54.5%). Future research is needed to help identify specific genetic and environmental factors underlying the dimensions of this heterogeneous disorder.

The specific genetic markers for OCD are largely unknown; however, genome-wide linkage studies that attempt to identify regions that may contain vulnerability genes have been conducted in patients with OCD. Early studies were conducted with small sample sizes and produced mixed results. Taken together, however, these early studies suggest that regions containing chromosome 9 may be of particular importance (Hanna et al., 2002; Shugart et al., 2006; Willour et al., 2004). Although these results are far from definitive, it is interesting to note that several studies have reported an association between OCD and a glutamate transporter gene (SLC1A1), which is located in the area of chromosome 9p (Chakrabarty, Bhattacharyya, Christopher, & Khanna, 2005; Ting & Feng, 2008; Rotge et al., 2010). More recently, however, Mathews and colleagues (2012) conducted a genome-wide linkage analysis using 33 families that had two or more individuals with childhood-onset OCD. Authors identified five areas of interest on chromosomes, with the strongest result on chromosome 1p36. Future studies are needed to replicate this genomic area of interest.

The etiology of BDD is also complex; however, extant research suggests that heritability is an important part of the variance of BDD etiology. A family study investigating the relationship between OCD and possible spectrum disorders revealed

that 8% of individuals with BDD have a first-degree relative with a lifetime diagnosis of BDD, which is 3 to 8 times greater than the prevalence in the general population (Bienvenu et al., 2000). Interestingly, 7% of patients with BDD also have a first-degree relative with OCD (Phillips, Gunderson, Mallya, McElroy, & Carter, 1998), and first-degree relatives of OCD patients have 6 times the lifetime prevalence of BDD compared to controls. Taken together, these studies suggest a shared heritability between BDD and OCD.

A recent twin study of BDD revealed that genetic factors accounted for 44% of the variance in dysmorphic concerns, whereas nonshared environmental factors accounted for the remaining variance (Monzani et al., 2012). Although there is limited research regarding specific genetic markers for BDD, one candidate gene study found association for GABA (A)-gamma-2 (5q31.1-q33.2) with the 1 (A) allele occurring more frequently in BDD subjects than controls (Phillips & Kaye, 2007). The GABA (A) receptor-y2 gene was also associated with BDD, but not OCD patients, in a subsequent genetic investigation (Richter et al., 2009).

Information regarding the etiology of HD is primarily derived from research on patients with OCD who have been divided into hoarding or nonhoarding subgroups. Within this framework, hoarding has been shown to have a strong familial association (Pertusa, Fullana, Singh, Menchon, & Mataix-Cols, 2008). In a study of monozygotic and dizygotic twins from the UK twin registry, "caseness" of hoarding was determined by completion of the Hoarding Rating Scale–Self Report (HRS-SR), with 2.3% of the sample reporting symptoms severe enough to be included (Iervolino et al., 2009). The authors found that heritability of hoarding in female twins was associated with both genetic (50%) and nonshared environmental factors (as well as measurement error). Shared environmental factors did not contribute to the liability. It is interesting to add that a significantly higher rate of severe hoarding, as well as any hoarding symptoms (compared to no symptoms), was observed for male twins, compared to female twins.

Given the recent inclusion of hoarding as a diagnostic category, there is little research in the area of genetic etiology of HD. Using data from a large collaborative genetics study of OCD, Samuels and colleagues (2007) found significant linkage of compulsive hoarding to Chromosome 14 in families with OCD. These investigators also found that hoarding and indecision were more prevalent in relatives of hoarding than nonhoarding OCD patients. Future research that focuses on HD as a separate diagnostic entity may help to increase understanding of etiological factors.

The etiology of TTM for any particular patient is most likely an interaction between biological, psychological, and social factors (Diefenbach, Reitman, & Williamson, 2000). Early genetic research indicates that hair-pulling behavior occurs at increased rates (5%–8%) in family members of TTM probands relative to normal controls (Christenson, Mackenzie, & Reeve, 1992; Lenane et al., 1992). Heritability has also been suggested by results of a twin study in which concordance rate for TTM (as defined by *DSM-IV-TR* criteria) was 38.1% for monozygotic twins compared to 0% for dizygotic twins (Novak, Keuthen, Stewart, & Pauls, 2009). Taken together, these studies suggest heritability is an important component in the etiology of TTM.

ED also appears to have a familial component. In a study with 60 patients with skin-picking disorder, Odlaug & Grant (2012) found 28.3% of first-degree family members also met criteria for the disorder. Another study found that 43% of 40 patients with ED

had first-degree relatives with skin-picking symptoms (Neziroglu, Rabinowitz, Breytman, & Jacofsky, 2008). Further in support of a heritability component in the etiology of ED, Monzani and colleagues (2012) found that clinically significant skin picking was reported by 1.2% of twins, with higher concordance for monozygotic than dizygotic twins. Within this female sample, genetic factors accounted for 40% of the variance, with the remaining variance attributable to nonshared environmental factors. Future studies are needed with homogenous samples, diagnosed with *DSM-5* criteria, to establish heritability of ED.

Neuroanatomy and Neurobiology

Extant literature supports an association between OCD and impairments of the brain's corticostriatal systems, which include organized neural circuits that connect the basal ganglia, thalamus, and cortex. For instance, fMRI findings suggest that patients with OCD exhibit impairments in functional connectivity of both the ventral and dorsal corticostriatal systems, with a direct link between ventral corticostriatal connectivity and symptom severity (Harrison et al., 2009). Although these authors were able to show system-wide differences in connectivity, the sample size was too small to determine the effects of specific symptom dimensions. More recent research has focused on a multidimensional model that examines direct links between major OCD symptom dimensions and structural and functional brain indicators (Menzies et al., 2010).

In a recent study, investigators evaluated the influence of OCD symptom dimensions on brain corticostriatal functional systems (Harrison et al., 2013). Results found a shared connectivity involving the ventral striatum and orbitofrontal cortex that was related to overall severity level, but independent of specific symptom dimensions. Rather, distinct anatomical relationships between the severity of symptom dimensions and connectivity were observed, with aggression symptoms moderating connectivity in the ventral striatum, amygdala, and ventromedial frontal cortex, and sexual/religious symptoms affecting ventral striatal-insular connectivity. This recent data suggests common pathophysiological changes in orbitofrontal-striatal regions across various forms of OCD. Further, Beucke and colleagues (2013) examined abnormal connectivity in the orbitofrontal cortex in medicated and nonmedicated OCD patients and matched normal controls. Consistent with previous research, the orbitofrontal cortex and the basal ganglia showed greater connectivity in unmedicated OCD patients, suggesting that antidepressant medication may reduce brain connectivity in OCD patients. It is also interesting to note that more distant connectivity was observed in this study, highlighting the need for future research to determine the extent of hyper connectivity outside of corticostriatal circuitry (Beucke et al., 2013).

Structural magnetic resonance imaging (MRI) studies with BDD patients have shown caudate nucleus asymmetry (Rauch et al., 2003) and orbitofrontal cortex volume abnormalities (Atmaca et al., 2010), with both studies finding an increase in white matter volume in patients with BDD. White matter microstructure was recently evaluated by diffusion weighted MRI to examine connectivity among structures thought to be involved in BDD (Feusner et al., 2013). Results of the study suggest a relationship between impairments in insight and fiber disorganization in tracts connecting visual with emotional and memory processing. Arienzo and

colleagues (2013) also conducted a brain network analysis and found disturbances in whole brain organization. Specifically, abnormal connectivity between regions involved in lower-order visual processing and higher-order visual and emotional processing was observed. Further, a study using single photon emission computed topography (SPECT) imaging found occipital perfusion and parietal abnormalities in BDD (Carey, Seedat, Warwick, van Heerden, & Stein, 2004), which is interesting as parietal dysfunction has also been shown to be associated with disturbances in body image (Trimble, 1988). Although more research is needed, these studies suggest disturbances in information processing in patients with BDD.

Given the perceived defects that patients with BDD report about their appearance, and the visuospatial processing deficits found within neuropsychological research, it is likely that disturbances in visual perceptual or visuospatial processing may be present in patients with BDD. In a neuroimaging study investigating visual processing of others' faces in patients with BDD compared to controls, fMRI was used to scan while subjects looked at photographs of unknown faces that were unaltered or altered to contain primarily low or high detail information (Feusner, Townsend, Bystritsky, & Bookheimer, 2007). BDD patients evidenced greater left hemisphere activity relative to controls for all image types but particularly to the low-detail faces. This laterality imbalance may suggest greater detailed facial processing and less holistic processing. In a more recent fMRI study, BDD subjects viewed photographs of their own face and a familiar face that had been altered or unaltered to include high or low detail information (Feusner, Neziroglu, Wilhelm, Mancusi, & Bohon, 2010). Again, BDD subjects showed relative hypoactivity in visual cortical systems for low detail photographs. To investigate if BDD patients have a more general abnormality in visual processing, BDD patients were scanned while looking at pictures of houses (as opposed to faces). The BDD group showed abnormal relative hypoactivity in left visual association areas for low detail images and hyperactivity of prefrontal systems for high detail images (Feusner et al., 2010). Thus, it appears that BDD patients may exhibit general abnormalities in lower and higher order visual processing.

Preliminary evidence suggests that hoarding symptoms may have a different neural substrate than OCD. Studies of animal hoarding and hoarding due to brain damage or dementia have implicated the subcortical limbic structures and the ventromedial prefrontal cortex as important in hoarding behavior (see Mataix-Cols, Pertusa, & Snowdon, 2011 for a review). Studies of humans with compulsive hoarding have focused on the same brain areas and found similar results. Saxena and colleagues (2004) found that compulsive hoarders show a unique pattern of abnormal resting-state brain function relative to that of normal controls and nonhoarding OCD patients. Specifically, the hoarding group evidenced abnormally low activity (reduced glucose metabolism) in the posterior cingulate cortex compared to normal controls and the dorsal anterior cingulate when compared to nonhoarding OCD patients.

Brain activity of hoarding and nonhoarding OCD patients was compared to normal controls in a symptom-provocation study (An et al., 2009). During an fMRI assessment, these subjects were asked to imagine throwing away objects that belonged to them while shown pictures of the items. The OCD patients with hoarding symptoms showed more reactivity in the ventromedial prefrontal cortex (VMPFC) than the other groups. In an exploratory study, Tolin, Kiehl, Worhunsky, Book, & Maltby (2009) conducted fMRI assessment of a small group of severe hoarders ($n = 12$; only 2 with

OCD diagnosis) and normal controls. When deciding whether to keep or discard real personal items, individuals with hoarding symptoms showed greater activity in the left lateral orbitofrontal cortex and parahippocampal gyrus compared to controls.

In a more recent study, neural activity was measured by fMRI in patients with well-defined primary HD (as proposed for *DSM-5* in Mataix-Cols et al., 2010) and compared to patients with OCD and normal controls (Tolin et al., 2012). The task involved real-time, binding decisions that had to be made about whether to keep or abandon actual belongings compared to control items. The HD group discarded significantly fewer personal items than the OCD and control groups with no differences in decisions to discard control items. With regard to neural activity, the HD group differed from OCD and normal controls in the anterior cingulate cortex and the left and right insular cortex. Taken together, these studies suggest that the ventromedial prefrontal/cingulate and medial temporal regions may be involved in hoarding behavior.

Imaging studies of TTM have been somewhat inconsistent. Early studies of hair pulling (then defined as an impulse control disorder NOS in *DSM-IV*) found evidence of fronto-striatal abnormalities (O'Sullivan et al., 1997; Keuthen et al., 2007) and fronto-striatal-thalamic pathways (Chamberlain et al., 2008). Structural abnormalities implicated increased grey matter densities in extensive areas including the prefrontal lobe, anterior cingulate, striatum, amygdala, and hippocampus (Chamberlain et al., 2008). In a subsequent study, Chamberlain and colleagues (2010) looked at white matter integrity, rather than gray matter abnormalities, using diffusion tensor imaging (DTI). Results indicated a disruption in white matter integrity in the anterior cingulate, orbitofrontal cortex, presupplementary motor areas, and temporal lobe compared to normal controls. These findings are, in part, similar to the findings in OCD patients described previously. In a recent study, white matter integrity was explored in patients with TTM and normal controls (Roos, Fouche, Stein, & Lochner, 2013). Although there were no differences between patients with TTM and controls on DTI measures, these investigators reported increased mean density (global average of all diffusion directions) in white matter tracts of the frontostriatal-thalamic pathway in patients with longer hair-pulling duration and increased TTM severity.

White matter abnormalities have also been shown in ED. Neurocognitive findings indicate that ED is related to impairment in prepotent motor responses and that this function is dependent on the integrity of the right frontal gyrus and the anterior cingulate cortices as well as the white-matter tracts that connect them. To examine whether these regions are impaired, Grant, Odlaug, Hampshire, Schreiber, & Chamberlain (2013) conducted a diffusion tensor imaging study with 13 subjects meeting proposed *DSM-5* criteria for ED. Results were as expected, with patients with ED showing significantly reduced fractional anisotropy in tracts distributed bilaterally, which included the anterior cingulate cortices. The findings support disorganization of white matter tracts involved in motor generation and suppression in the pathophysiology of excoriation in patients with ED.

LEARNING, MODELING, AND LIFE EVENTS

There is some evidence that trauma may be associated with increased symptom severity in OCD (Cromer, Schmidt, & Murphy, 2007). Among children and

adolescents, OCD is related to an increased number of lifetime traumatic events as well as more events in the year preceding onset, compared to those with any other anxiety disorder (Gothelf, Aharonovsky, Horesh, Carty, & Apter, 2004). The severity of childhood trauma also appears to be greater for patients with OCD compared to normal controls (Lochner, du Toit, et al., 2002). Other life events associated with OCD onset include accidents and serious mistakes (Rheaume, Freeston, Leger, & Ladouceur, 1998) as well as pregnancy and childbirth (Wisner, Peindl, Gigliotti, & Hanusa, 1999).

Developmental factors, particularly sexual, emotional, and physical abuse, may be associated with BDD. Although no longitudinal data is available, two cross-sectional studies found frequent reports of childhood maltreatment in BDD cases. Neziroglu, Khemlani-Patel, and Yaryura-Tobias (2006) found that 19 of 50 BDD patients (38%) reported some type of abuse during childhood (28% emotional abuse, 22% sexual abuse, and 14% physical abuse) compared to 14% of a group of 50 patients with OCD. Early abuse was shown to be associated with BDD in another study (Didie et al., 2006) with nearly 79% of 75 BDD subjects reporting a history of maltreatment (68% emotional neglect, 56% emotional abuse, 33.3% physical neglect, and 28% sexual abuse).

Early social interactions with peers may also be associated with BDD. In one study, individuals with BDD reported more teasing by peers, especially about appearance, compared to healthy control subjects (Buhlman, Cook, Fama, & Wilhelm, 2006). In a recent study appearance-related social-evaluative concerns were higher in BDD patients than healthy controls (Anson, Veal, & de Silva, 2012). Specifically, BDD participants reported higher levels of importance and anxiety associated with perceptions of others' view of their appearance as well as their own view.

It has been suggested that HD may develop as a conditioned emotional response related to thoughts or beliefs concerning items or possessions (Grisham & Barlow, 2005). Anxiety experienced with discarding and decision-making is avoided by acquisition and hoarding of items. Furthermore, the hoarding behavior is reinforced because the possessions take on pleasurable or soothing characteristics; however, more research is needed in this area.

TTM and ED may have similar environmental risk factors. Lack of stimulation or boredom has been suggested as a factor in both experimental (Teng, Woods, Marcks, & Twohig, 2004) and self-report studies (Shusterman, Feld, Baer, & Keuthen, 2009; Snorrason, Smári, & Olafsson, 2010). Early case reports also suggested that severe activity restriction may be implicated in the development of TTM and ED (Evans, 1976; Gupta, Gupta, & Haberman, 1986). Further, a number of case studies have suggested a relationship between history of trauma and skin picking/hair pulling but longitudinal data are needed to determine whether traumatic events play a causal role in these disorders (Snorrason, Belleau, Woods, 2012).

Cognitive Influences

A cognitive model of OCD (Rachman, 1997) proposes that it is not the content of the intrusive thought per se, but the interpretation of the thought that leads to preoccupation and anxiety in patients with OCD. In this model, dysfunctional beliefs about the inability to tolerate the negative emotions associated with the intrusive thoughts are thought to lead to the development and maintenance of OCD. Three

types of dysfunctional beliefs have been proposed to contribute to OCD: (1) overestimated responsibility and exaggerated threat; (2) perfectionism and intolerance of uncertainty; and (3) overimportance of thoughts and need to control thoughts (Calkins, Berman, & Wilhelm, 2013).

In a large, nonclinical sample, Taylor and colleagues (2010) used structural equation modeling and found that responsibility and threat estimation beliefs predicted all types of OCD (checking, hoarding, ordering, washing) above and beyond the other two types of beliefs. Using an assessment instrument that conceptualizes OCD from a multidimensional perspective, Wheaton, Abramowitz, Berman, Riemann, and Hale (2010) replicated this finding in a clinical sample, with beliefs related to inflated responsibility and threat predicting contamination and responsibility for harm dimensions. However, other symptom dimensions were predicted by other beliefs, with each dimension of OCD uniquely predicted by a single belief domain. The results of this study and others indicate intolerance of uncertainty to predict OC symptoms (Boelen & Carleton, 2012; Carleton et al., 2012), which highlights the importance of investigating OCD as a multidimensional, heterogeneous disorder.

Neurocognitive performance in OCD patients has received considerable attention, with impairment in executive functioning a common finding. Early examples of executive dysfunction include studies that showed decreased cognitive flexibility and set shifting (Henry, 2006; Lawrence et al., 2006) and impaired decision-making and planning (Shin et al., 2004). Memory impairments in tests requiring implicit organization have also been demonstrated (Greisberg & McKay, 2003). In a recent study, Kashyap, Kumar, Kandavel, and Reddy (2013) tested neuropsychological functions in 150 patients with OCD compared to 205 healthy control subjects. Patients with OCD showed deficits in scanning, planning time, concept formation, decision-making and encoding of nonverbal memory. Thus, these results confirm executive dysfunction, with particular difficulties in strategizing and organizing. Of note, this neuropsychological profile involves the prefrontal cortex and striatum, suggesting that OCD may not be just an orbitofronto-striatal disorder.

Cognitions in BDD are similar to those in OCD in that patients with BDD experience recurrent, persistent, and intrusive preoccupations. In BDD, however, these thoughts are specifically related to perceived physical defects. There have been fewer studies that have examined neurocognitive functioning in patients with BDD. However, like patients with OCD, most studies have suggested executive dysfunction. Specifically, Hanes (1998) compared patients with BDD, OCD, and schizophrenia to normal controls on tests of executive function, memory, and motor function. BDD and OCD patients showed more impaired performance on executive function tasks (New Tower of London and Stroop) compared to controls, suggesting impairment in the frontal cortex. Similarly, patients with BDD showed both nonverbal (Rey Complex Figure Test) and verbal (California Verbal Learning Test) memory impairments when compared to healthy controls (Deckersbach et al., 2000). The authors suggest that the memory impairments may be mediated by poor organizational strategies, possibly as a result of executive dysfunction.

More recently, Dunai, Labuschagne, Castle, Kyrios, and Rossell (2010) again demonstrated executive functioning deficits in patients with BDD, specifically deficits related to spatial working memory and thinking speed. However, in this study, patients with BDD did not show deficits in short-term memory capacity, motor speed,

or visual memory, which may be due to heterogeneous executive function measures used in the different studies. In a recent study, authors compared executive function in BDD and OCD patients using the same cognitive tasks for both groups (Spatial Span, Spatial Working Memory, Stockings of Cambridge, and Pattern Recognition). In general, results suggest that both groups evidence impaired executive functioning compared to controls (Labuschagne, Rossell, Dunai, Castle, & Kyrios, 2013); however, there was also an interesting difference between groups, as BDD patients showed greater deficits on a planning task that assesses spatial planning ability, compared to both OCD patients and controls.

There is less known about the significance of cognitions in HD. Most research has focused on indecisiveness and emotional attachment to objects. In general, impairment in decision-making has been thought to be a core feature of HD. Results of early neuropsychological research are mixed and interpretation is difficult, as different tasks with homogeneous groups have been used (Grisham, Brown, Savage, Steketee, & Barlow, 2007; Hartl et al., 2004; Lawrence et al., 2006). More recently, Grisham, Norberg, Williams, Ceroma, and Kadib (2010) used a well-standardized neuropsychological battery to assess severe hoarders, matched anxious, and matched normal controls. In this study, severe hoarders showed deficits on only the planning/problem-solving task and did not differ on tasks of decision-making, cognitive flexibility, or response inhibition. Further, Frost, Tolin, Steketee, and Oh (2011) examined indecisiveness in a large sample of adults who self-referred as having severe hoarding. Interestingly, they also examined hoarding in adult children and spouses of these individuals. Individuals with hoarding problems reported more decision-making problems than children or spouses and substantially more than normal controls. In addition, adult children reported more indecisiveness than spouses, suggesting a familial characteristic.

Memory problems have also been implicated in this population, as compulsive hoarders have been shown to score significantly worse on tasks of implicit memory (Blom et al., 2011). Tolin and colleagues (2011) found decreased ability to sustain attention and poorer adaptive memory strategies in patients with HD relative to OCD and normal controls. The authors note that true impairment on any neuropsychological task was rather low across all groups; however, 67% of hoarders (compared to 58% of OCD and 42% of normal controls) scored in the impaired range on at least one measure (Tolin et al., 2011). Finally, executive functioning has been assessed in older adults with HD (Ayers et al., 2013). Matched for age with healthy controls, older adults showed impaired functioning in executive function including working memory, mental control, inhibition, and set shifting. More research is needed to replicate these findings with homogeneous groups under similar conditions.

With regard to ED, research regarding cognitive influences and neuropsychological functioning is needed due to its recent inclusion in the *DSM-5*.

Sex and Racial-Ethnic Considerations

Men and women are equally likely to suffer from OCD, although community samples evidence higher rates in women, whereas clinical samples evidence higher rates of OCD in men (Karno, Golding, Sorenson, & Burnam, 1988). These contradictory findings suggest that men may experience more impairment related to OCD symptomology,

which may lead to increased help-seeking behavior. In a recent comprehensive cross-sectional study conducted in Brazil, phenomenological characteristics of men and women with OCD were evaluated (Torresan et al., 2013). The sample included 504 women (58.7%) and 354 men (41.3%) with a mean age of 35.4 years old (18-77). Men were found to be younger, more frequently single, and with symptom interference at a younger age. In addition to these differences, the obsessional content in men was more likely to encompass sexual/religious themes, whereas women were more likely to present with symptoms related to aggression, contamination/cleaning, and hoarding. Results of this study support results found in studies previously conducted in Italy (Lensi et al., 1996) and India (Khandelwal, Aggarwal, Garg, & Jiloha, 2009).

Contamination and checking are OCD themes most consistently found across cultures (Matsunaga & Seedat, 2007). Other specific themes or content of OCD symptoms may be more prevalent in certain cultures, such as fear of leprosy among those who live in Africa (Steketee & Barlow, 2002) or religion themes among those from the Middle East (Fontenelle, Mendlowicz, Marques, & Versiani, 2004). There is some data that suggests lower prevalence of OCD among African Americans (Karno et al., 1988) although this may reflect lower numbers of African Americans seeking evidence-based treatments in mental health settings. An underrepresentation of minorities in clinical trials of evidence-based treatments suggests that efficacy in non-White populations is not known (Williams, Powers, Yun, & Foa, 2010).

In an early study of BDD, Bohne, Keuthen, Wilhelm, Deckersbach, & Jenike (2002) found similar rates of body dysmorphic concerns in German (5.3%) and American (4%) students, which may be expected due to somewhat similar cultures of the two countries. In a cross-sectional study of BDD in undergraduates in the southeast United States, differences in gender, race/ethnicity, and sexual orientation were evaluated. In this population, an overall BDD prevalence of 4.9% was obtained, with women endorsing more symptoms of BDD than men. In addition, among women, Caucasians and Latinas endorsed more symptoms than African Americans, and sexual minorities of both genders endorsed more symptoms than heterosexuals (Boroughs, Krawczyk, & Thompson, 2010). Further, racial/ethnic factors in BDD were assessed in an online survey (Marques et al., 2011). In this study, no significant differences were found between Caucasian, Latino, or African American participants. However, there was a significant difference between Caucasian and Asian participants, with Asians reporting more concern with straight hair and dark skin, but fewer body shape concerns. In addition, Asian respondents reported lower rates of grooming, touching body parts, and camouflaging, as well as higher rates of exercise. It is important to note that this research is in the early stages and has focused on BDD symptoms rather than BDD in clinical settings.

Two studies have shown compulsive hoarding to be more prevalent in women (Iervolino et al., 2009; Samuels et al., 2008); however, the phenomenology of hoarding is very similar in men and women. Although most research has been done with OCD populations, subdivided into hoarding and nonhoarding groups, there is no data suggesting that hoarding is different across cultures (Mataix-Cols et al., 2010). Obviously more research is needed in this area now that HD is a standalone diagnosis in *DSM-5*.

Existing literature indicates that 88 to 94% of patients with TTM are female (Odlaug, Kim, & Grant, 2010). The reason for this large gender bias is unclear, but may be related to societal values of beauty, and related distress, and greater drive to seek help due to hair loss in women. There is very little research regarding racial/ethnic differences in TTM. In a survey of American college students, there was no difference found between African-American and non-African students (McCarley, Spirrison, & Ceminsky, 2002). In a more recent study, ethnic differences in TTM symptoms were evaluated among minority and Caucasian participants (Neal-Barnett et al., 2010). Overall, results indicate that the minority sample was less likely to report pulling from eyebrows and eyelashes, as well as less likely to report tension prior to pulling. There was also a difference in interference, in which minorities reported more problems with home management related to pulling, and Caucasians reported more interference with academic endeavors. In addition, Caucasians reported more daily stress and treatment utilization, although treatment efficacy did not differ among ethnic groups.

ED is more frequent in females with higher rates of co-occurring grooming disorders (Grant et al., 2012). The clinical characteristics have been shown to be the same across age ranges as well as cultures (Bohne et al., 2002; Lochner, Simeon, Niehaus, & Stein, 2002).

Course and Prognosis

OCD is a chronic and disabling disorder that rarely remits without treatment. The development of OCD usually begins between late adolescence and early adulthood. Symptoms of OCD are typically stable over time, with changes occurring within symptom dimensions rather than between symptom dimensions (Mataix-Cols et al., 2002). In a recent multicenter naturalistic study from the International College of Obsessive Compulsive Spectrum Disorders (ICOCS), early onset and long duration of illness were identified as negative predictors of long-term outcome (Dell'Osso et al., 2013).

Both biological and behavioral therapies have been shown to be effective. Positive treatment outcome has been shown with SSRIs (such as Prozac or Zoloft) as well as cognitive-behavioral treatments, such as exposure with response-prevention (ERP) (NICE, 2006). In a recent meta-analysis, Olatunji, Davis, Powers, and Smits (2013) evaluated 16 randomized controlled trials (RCTs) of CBT for OCD and found that CBT outperformed control conditions across the studies. Of greater interest, perhaps, is that few moderator variables affected efficacy. Specifically, outcome was not associated with greater severity of OCD or level of depression at pretreatment. There were smaller effect sizes for adult RCTs and older age, suggesting greater efficacy in younger patients with OCD. CBT should be considered a first-line treatment for OCD, with or without adjunctive pharmacotherapy.

BDD typically begins in adolescence (Phillips et al., 2005), which is a stage of development marked by hormonal changes and accelerated growth. Adolescence is also a period in which acne may develop and lead to peer rejection. These factors may be related to, or trigger, the development of BDD, but research is needed to address these factors. A recent study compared patients with early onset BDD (before age 18) to later onset BDD (Bjornsson et al., 2013). In general, early onset was associated with more gradual onset, a lifetime history of attempted suicide, and greater comorbidity.

With regard to treatment, efficacy of cognitive behavior therapy for BDD has recently been reviewed (Prazeres, Nascimento, & Fontenelle, 2013). Authors indicate that both individual and group cognitive behavioral therapies, that include psychoeducation, cognitive restructuring, and ERP, are superior to no treatment.

It has been suggested that HD may develop in response to early deprivation, both emotional and material, but this has not been largely supported (Frost & Gross, 1993). Studies have shown abnormally high levels of trauma or stressful life events that, in some cases, occur prior to the onset or worsening of symptoms (Cromer, Schmidt, Murphy, 2007; Samuels et al., 2008). However, hoarding is a chronic disorder and there is no evidence that hoarding can be explained as a response to stressors or losses (Mataix-Cols et al., 2010). The course of compulsive hoarding is typically chronic with hoarding behavior beginning decades before symptoms reach a clinical level (Samuels et al., 2008). No prospective studies have been completed but retrospective data suggest that hoarding symptoms begin in childhood or early adolescence (Ayers, Saxena, Golsha, & Wetherell, 2009) and begin interfering with daily life by the mid-30s (Pertusa et al., 2008). It has also been suggested that acquisition has a later onset than difficulty discarding or clutter (Grisham, Frost, Steketee, Kim, & Hood, 2006), possibly due to means to acquire and a place to store possessions.

Treatment of compulsive hoarding has been described as challenging due to low levels of insight, little motivation for treatment, and impaired cognitive functioning (Grisham & Barlow, 2005). In patients with OCD, the presence of hoarding symptoms is typically associated with refusal of treatment and higher dropout rates. Cognitive behavioral treatment, usually involving psychoeducation, practice in decision making, and exposure components, is generally thought of as the treatment of choice for hoarding. Randomized controlled trials are needed for this recently defined disorder.

TTM may occur at any age, from infancy through later life. Most research, however, indicates an average age of onset at 12.9 years (Cohen et al., 1995; Grant, Odlaug & Kim, 2010; Lochner et al., 2010; Odlaug & Grant, 2008). TTM may interfere with social relationships, family life, and work, and has been associated with significant impairment (Woods et al., 2006). Although there are studies on the long-term course of the disorder, most data suggest that the course is chronic, with waxing and waning symptom severity (Snorrason, Belleau, Woods, 2012). With regard to treatment, Flessner, Penzel, and Keuthen (2010) have identified cognitive-behavioral treatment as the treatment of choice for TTM. Although Habit Reversal Training (Azrin, Nunn, & Frantz, 1980) was initially posited as effective for TTM, failure to achieve greater symptom reduction, with longer lasting effects, has led researchers to look at inner experiences that may trigger hair pulling.

Experiential avoidance has been associated with more severe hair pulling and fear of negative evaluation (Norberg, Wetterneck, Woods, & Conelea, 2007). Woods and colleagues have evaluated the addition of Acceptance and Commitment Therapy (ACT) to traditional habit reversal and have shown significant reductions in hair pulling that persisted to 3-month follow-up (Twohig & Woods, 2004; Woods, Wetterneck, & Flessner, 2006). Affective dysregulation has also been evaluated as playing a role in TTM (Shusterman et al., 2009). Dialectical Behavior Therapy (DBT; Linehan, 1993a, 1993b) has also been combined with habit reversal training with positive results. In a series of trials, Keuthen and colleagues have demonstrated an

inverse relationship between hair pulling severity and emotional regulation that has persisted at both 3- and 6-month follow-up (Keuthen et al., 2010; Keuthen et al., 2011; Keuthen et al., 2012). Given these promising results, DBT-enhanced CBT for TTM should be evaluated against other credible treatment interventions and at longer follow-up.

Research suggests that the age of onset for skin picking varies considerably, with onset from childhood through adulthood. Most research has shown an age of onset from 12 to 16 years, with an average age across studies of 13.5 years (Flessner & Woods, 2006; Grant et al., 2007; Grant, Odlaug & Kim, 2010; Lochner et al., 2002). Symptoms appear to be similar regardless of age and no differences have been reported in different cultures (Grant et al., 2012). The course of the disorder is also variable with most cases being chronic in nature with fluctuating intensity. Patients usually pick on a daily basis, often for a significant amount of time, and severity tends to vary with life stressors (Snorrason, Stein, Woods, 2013). Skin problems may occur, including bleeding and soreness, with possibility of infection or permanent skin damage.

Individuals with ED may experience mild to severe impairment in social, academic, or occupational functioning. Treatment has largely focused on cognitive-behavioral interventions and pharmacology (SSRIs). Habit reversal training has been used (Deckersbach et al., 2002), as well as habit reversal combined with acceptance and commitment therapy (Siev, Reese, Timpano, & Wilhelm, 2012; Woods, Wetterneck, et al., 2006), both with promising results. Emotion dysregulation has been suggested to be a factor in ED, which may lead to future research on treatment using DBT procedures in conjunction with traditional CBT.

Case Studies

Ann is a 34-year-old female who is consumed by thoughts of germs, contamination, and sickness. She is constantly fearful that she may encounter bacteria or a virus that will cause her to become ill and ultimately lead to her death. She experiences intrusive images of herself lying in a hospital bed and of her own funeral. Despite attempting to disregard these thoughts and images, Ann is unable to control her need to clean and sterilize her surroundings to ensure she does not come into contact with germs. Ann spends hours each day cleaning and disinfecting her home, often recleaning areas she has just cleaned. She no longer allows friends or family to enter the home in an effort to protect herself. Ann rarely leaves the house, except to purchase cleaning supplies or go to medical appointments. She is no longer able to work, experiences significant financial strain, and has little to no social life.

Tanya is a 22-year-old female who is preoccupied with the shape of her face. She spends hours per day gazing into the mirror criticizing the odd shape of her face, mentally commenting on the asymmetrical angles of her cheekbones, the sharp point of her chin, and the uneven hairline above her forehead. Friends and family are unaware of her preoccupation and believe that she is an ordinary, even attractive, looking female. Aside from spending hours critiquing herself in the mirror, Tanya is constantly comparing her facial features to others around her, noting how pronounced her perceived defects are compared to the perfection of others' facial shapes. Despite her attempts to hide the perceived flaws using hairstyles, scarves, and makeup, Tanya begins to experience passive suicidal ideation.

Jack is a 67-year-old retired, widowed male. He spends the majority of his time shopping at garage sales, exploring dumpsters for what he calls "treasures," and shopping online. Despite an excessive accumulation of items, Jack is unable to discard anything in his home to make room for his new purchases. In fact, he experiences such difficulty parting with items, even boxes, newspapers, and broken tools, that he has little room left in his home to live. Despite the urging of his family to de-clutter his home and curb his shopping, Jack is unable to make the necessary changes due to the distress he experiences attempting to make the changes. As a result, he is experiencing significant strain in his familial relationships and is at risk of losing his home due to his inability to maintain city health codes.

Jess is a 29-year-old female who presented to her primary care doctor due to frequent hair pulling. Specifically, Jess reported that she finds herself pulling hairs out of her scalp throughout the day, most frequently when engaged in stressful activities such as difficult work assignments. Initially, Jess was pulling out her hair infrequently; however, she has begun to notice bald spots above her ears, where she pulls most frequently. People at work have begun to comment on the hair loss, asking if she is okay. She is very distressed by her behavior, and the attention it brings from others, but is experiencing difficulty stopping.

Tim is an 18-year-old male who frequently engages in skin picking. Specifically, Tim began by picking at an ingrown hair on his leg, which quickly progressed to picking at normal skin, lesions, and scabs all over his body. Initially, Tim used his fingernails to pick, but has recently begun using tweezers, knives, and toothpicks. Although he feels embarrassed by the scars, some of which are infected, Tim feels as though he is unable to stop picking. His girlfriend of 2 years has been threatening to break up if he does not get some help.

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CHAPTER 10

Trauma and Stressor-Related Disorders

Posttraumatic Stress Disorder, Acute Stress Disorder, and Adjustment Disorders

ANOUK L. GRUBAUGH

THE *DIAGNOSTIC AND Statistical Manual of Mental Disorders*, fifth edition (*DSM-5*; American Psychiatric Association [APA], 2013) includes a chapter titled "Trauma and Stress-Related Disorders," which contains posttraumatic stress disorder (PTSD), acute stress disorder (ASD), and the adjustment disorders. Both PTSD and ASD were previously classified under the "Anxiety Disorders" chapter of the *DSM-IV*, whereas adjustment disorders were classified separately as a residual diagnostic category (APA, 1994). PTSD is broadly characterized as a psychiatric disorder resulting from a life-threatening event and requires a history of exposure to a traumatic event (Criterion A) that results in a minimum threshold of symptoms across four symptom clusters: intrusion, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity (Criterion B through E). Additional criteria concern duration of symptoms (Criterion F), functioning (Criterion G), and differential diagnosis due to a substance or other co-occurring condition (Criterion H).

For Criterion A, an event associated with PTSD must include actual or threatened death, serious injury, or sexual violation resulting from one or more of the following scenarios:

- Directly experiencing the traumatic event.
- Witnessing the traumatic event in person.
- Experiencing the actual or threatened death of a close family member or friend that is either violent or accidental.
- Directly experiencing repeated and extreme exposure to aversive details of the event (i.e., the type of exposures frequently encountered by police officers and first responders).

With regard to criteria B through E, an individual must report symptoms from each of the four symptom clusters. *Intrusion symptoms* (Criterion B) include repetitive, involuntary, and intrusive memories of the event; traumatic nightmares; dissociative reactions (i.e., flashbacks) along a broad continuum; intense prolonged distress after exposure to reminders of the trauma; and heightened physiological reactivity to reminders of the trauma. *Avoidance symptoms* (Criterion C) include avoidance of trauma-related thoughts or feelings; and avoidance of people, places, activities, and so forth that cue distressing thoughts or feelings about the traumatic event. *Negative alterations in cognitions and mood symptoms* (Criterion D) include a persistent and distorted sense of self or the world; blame of self or others; persistent trauma-related emotions such as anger, guilt, shame; feeling estranged or detached from others; marked lack of interest in pretrauma activities; restricted range of affect; and difficulty or inability remembering important parts of the traumatic event. Finally, *alterations in arousal and reactivity symptoms* (Criterion E) include irritability and aggressiveness self-destructive or reckless behaviors, sleep difficulties, hypervigilance, marked startle response, concentration difficulties, and sleep disturbance.

For a diagnosis of PTSD an individual must exhibit at least one symptom from Criterion B, one symptom from Criterion C, two symptoms from Criterion D, and two symptoms from Criterion E, and the symptoms endorsed in categories B through E must persist for 1 month or longer (Criterion F). The symptoms must also be accompanied by significant distress or impairment in social, occupational, or other important life domains (Criterion G), and symptoms cannot be better explained by another medical or psychiatric illness (Criterion H).

The *DSM-5* includes two additional specifiers or associated features that can be added to a PTSD diagnosis: "with dissociated symptoms" and "with delayed expression." The dissociated symptoms specifier includes either *depersonalization* (i.e., experience of being an outside observer to one's experience or feeling detached from oneself) or *derealization* (i.e., experience of unreality or distortion) in response to trauma-related cues. The delayed onset specifier includes an onset of symptoms that can occur immediately after the trauma, but that may not meet full criteria for PTSD until at least six months after the trauma.

Some notable changes were made to the diagnostic criteria for PTSD from *DSM-IV* (APA, 1994) to *DSM-5*. In addition to the inclusion of specifiers for depersonalization and derealization, the *DSM-5* provides greater specification regarding what events constitute a traumatic event (i.e., what events constitute a Criterion A event); and excludes the need for an individual to have experienced intense fear, helplessness, or horror at the time of the trauma due to its lack of predictive utility. Additionally, the avoidance/numbing symptom cluster found in the *DSM-IV* is divided into two distinct clusters in the *DSM-5*: *avoidance* and *negative alterations in cognitions and mood*. The latter of these clusters retain most of the *DSM-IV* numbing symptoms while also including a broader range of emotional reactions. Last, Criterion E, alterations in arousal and reactivity, retains the majority of *DSM-IV* arousal symptoms but also includes additional symptoms regarding aggressive or reckless behavior.

A diagnosis of acute stress disorder (ASD) requires an antecedent event (Criterion A event) in which the person:

- Experienced an event or events that involved a threat of death, actual or threatened serious injury, or actual or threatened physical or sexual violation.

- Witnessed an event or events that involved the actual or threatened death, serious injury, or physical or sexual violation of others.
- Learned of such harm coming to a close relative or friend.
- Experienced repeated or extreme exposure to aversive details of unnatural death, serious injury, or serious assault or sexual violation of others that were not limited to electronic media, television, video games, and so forth.

Individuals must then exhibit a minimum of 9 out of 14 symptoms across a broad spectrum of posttraumatic reactions (Criterion B). This spectrum includes symptoms related to negative mood, intrusive thoughts, dissociation, avoidance, and anxiety. Aside from a greater emphasis on dissociative symptoms, the other Criterion B symptoms for ASD largely mirror the Criterion B through E symptoms for PTSD. Additional criteria for ASD concern duration of symptoms (Criterion C), functioning (Criterion D), and differential diagnosis due to a substance or other co-occurring condition (Criterion E).

Changes to the diagnostic criteria of ASD from *DSM-IV* to *DSM-5* include less emphasis on dissociative criteria (i.e., feeling detached from one's body, emotions, or the world). Rather than being required for a diagnosis as was the case in the *DSM-IV*, dissociative symptoms in *DSM-5* are viewed as one of several possible posttraumatic reactions that an individual may experience. Comparable to changes to the diagnostic criteria for PTSD, the *DSM-5* provides more specification regarding the qualifying traumatic event for ASD; and the criterion requiring a subjective reaction to the trauma (i.e., fear, helplessness, horror) was eliminated.

Adjustment disorders are classified in the *DSM-5* as a range of stress response syndromes. This differs from the *DSM-IV* in which adjustment disorders were part of a residual category for individuals experiencing clinically significant distress that did not fit diagnostic criteria for other psychiatric disorders. Specific *DSM-5* criteria for an adjustment disorder include: (a) the development of emotional or behavioral problems in response to an identifiable stressor occurring within 3 months of exposure to the stressor (this feature is considered the core feature of adjustment disorders; (b) symptoms or behaviors are clinically significant and out of proportion to the severity of the stressor once cultural and contextual factors are taken into account. Additionally, the stress response (a) cannot be better accounted for by another disorder and is not an exacerbation of a preexisting condition; (b) is not indicative of normal bereavement (if this is the precipitating event); and (c) once the stressor is removed, the symptoms do not persist for more than 6 additional months. Diagnostic specifiers for the adjustment disorders include depressed mood, anxiety, mixed anxiety and depressed mood, disturbance of conduct, mixed disturbance of emotions and conduct, and unspecified.

Whereas PTSD and ASD emphasize fear and anxiety responses, adjustment disorders can accommodate a broader range of stress reactions. Second, although there is an explicit potential for ASD to predict subsequent impairment (i.e., to predict the development of PTSD), an adjustment disorder is typically viewed as a discrete disorder that has a fairly immediate onset and is relatively short in duration. A third distinction between PTSD, ASD, and adjustment disorders regards the timing of diagnosis. Adjustment disorders can be diagnosed immediately after the event, ASD can be diagnosed from 2 days to up to 1 month after the event, and PTSD can be diagnosed from 1 month to several years after the trauma.

CLINICAL FEATURES

The clinical expression of PTSD can vary significantly in terms of severity. Although the diagnosis is categorical, there is evidence of a dimensional structure to PTSD (Broman-Fulks et al., 2006; Forbes, Haslam, Williams, & Creamer, 2005; Ruscio, Ruscio, & Keane, 2002). An implication of this dimensional structure is that milder symptoms of PTSD may cause significant distress and impairment. Indeed, one study found that veterans with subthreshold PTSD underutilize mental health care, despite increased psychiatric comorbidity and impairment relative to veterans without PTSD (Grubaugh et al., 2005). Yet other studies using samples of Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) veterans have found an association between subthreshold PTSD and elevated levels of anger and hostility, physical health functioning, and an increased likelihood of hopelessness and suicidal ideation relative to those without PTSD (Jakupcak et al., 2011). Among civilians, subthreshold PTSD has likewise been associated with levels of impairment and suicidality that are equivalent to those with full PTSD (Zlotnick, Franklin, & Zimmerman, 2002).

Suicidality is elevated among individuals with PTSD (Panagioti, Gooding, & Tarrier, 2009; Jakupcak et al., 2011), and particular types of trauma, such as childhood abuse, military sexual trauma, and combat, may be more strongly associated with suicidality than others (Afifi et al., 2008; Kimerling, Gima, Smith, Street, & Frayne, 2007). Additionally, increased risk of suicidality is uniquely associated with PTSD (Sareen, Houlahan, Cox, & Asmundson, 2005; Sareen et al., 2007). That is, this association is not solely accounted for by the presence of other psychiatric conditions commonly found with PTSD. Of course, an increased risk of suicidality is present in a number of other psychiatric conditions to a comparable or greater degree than that found in PTSD (Nock, Hwang, Sampson, & Kessler, 2010).

The clinical picture of acute stress disorder (ASD) is similar to that of PTSD. Additionally, a review on the topic found that at least half of trauma survivors with ASD subsequently met criteria for PTSD (Bryant, Friedman, Spiegel, Ursano, & Starin, 2011). This finding suggests that individuals with ASD are, in fact, at higher risk of subsequently developing PTSD. Conversely, however, the majority of individuals who subsequently develop PTSD do not initially meet criteria for ASD, suggesting that ASD (using *DSM-IV* criteria) is not highly specific with regard to its predictive utility. Additional findings suggest that the predictive power of ASD is increased when subthreshold symptoms are used and the dissociative symptoms required for *DSM-IV* are relaxed (Bryant et al., 2011). These and similar findings likely influenced the decreased emphasis in *DSM-5* on dissociation symptoms in favor of accepting a broader symptom presentation and one that more closely mirrors the symptoms associated with PTSD.

Due to the conceptualization of adjustment disorders as fairly time limited, as well as their history as a nebulous, catch-all diagnostic category, they have not been well studied in the psychiatric literature. The findings that do exist largely consist of non-U.S. samples, focus on children or adolescents, and/or were published in the 1980s and early 1990s. Some commonly agreed upon emotional signs of adjustment disorders are sadness, hopelessness, lack of enjoyment, crying spells, nervousness, anxiety, worry, trouble sleeping, difficulty concentrating, feeling overwhelmed, and thoughts of suicide. Some behavioral signs of adjustment disorders include

fighting, reckless behaviors, neglecting important tasks or responsibilities, and avoiding family or friends. Although the presence of an adjustment disorder has been linked to increased suicidal ideation and risk of suicide (e.g., Portzky, Audenaert, & Vanheeringen, 2005; Taggart et al., 2006), they are often considered less severe than other psychiatric disorders. Supporting this view, one study found that adjustment disorders range in severity between no psychiatric disorder and the presence of a mood or anxiety disorder (Fernandez et al., 2012).

DIAGNOSTIC CONSIDERATIONS

Comorbidity is a concern when diagnosing PTSD. Large nationally representative samples have found that PTSD is significantly correlated with the majority of mood and anxiety disorders, as well as alcohol use disorders (National Comorbidity Survey Replication [NCS-R]; Kessler, Chiu, Demler, & Walters, 2005; National Comorbidity Survey [NCS]; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995). Data from the NCS-R found that approximately half of those who met criteria for PTSD also met criteria for *at least* three additional psychiatric diagnoses (Kessler et al., 1995). Although there is some degree of symptom overlap between PTSD and other psychiatric diagnoses (e.g., sleep and concentration difficulties and diminished interest in activities are common to both depression and PTSD), this overlap does not account for the high rate of comorbidity (Elhai, Grubaugh, Kashdan, & Frueh, 2008). When comorbid with mood disorders, PTSD is more likely to be primary, whereas it is more likely to be secondary when comorbid with anxiety disorders (Kessler et al., 1995). Importantly, PTSD and comorbid diagnoses may change over time within a given individual. A study of trauma survivors found that half of those who reported PTSD only at 3-month follow-up reported depression only at 12-month follow-up; likewise, half of those with depression only at 3-month follow-up reported PTSD only at 12-month follow-up (O'Donnell, Creamer, & Pattison, 2004).

Due to the lack of epidemiological studies specific to ASD or the adjustment disorders, there are few reliable data on the clinical comorbidity associated with these disorders. Given the conceptual overlap between ASD and PTSD, it is likely that individuals with ASD experience high rates of mood, anxiety, and substance disorders relative to the general population, as well as an increased risk of suicidality. As noted elsewhere, adjustment disorders in the *DSM-IV* served as a residual "catch-all" diagnostic category once other psychiatric conditions were ruled out. As such, they are seldom diagnosed with other psychiatric conditions. With this restriction in mind, adjustment disorders have most often been linked in adult samples to a comorbid diagnosis of a personality disorder, substance use disorder, and increased suicidality (Dowrick et al., 1998; Greenberg, Rosenfeld, & Ortega, 1995; Polyakova, Knobler, Ambrumova, & Lerner, 1998; Strain et al., 1998).

EPIDEMIOLOGY

In the general population, the 12-month and lifetime prevalence of PTSD is 3.5 and 6.8%, respectively (Kessler, Burglund, Demler, et al., 2005; Kessler et al., 2005). Point prevalence of PTSD among U.S. combat veterans is estimated to be between 2% and

17%, depending on the characteristics of the sample and the measurement strategies that were used (Richardson, Frueh, & Acierno, 2010). There are different conditional probabilities of developing PTSD by trauma type. For example, combat exposure and physical and sexual abuse are more often associated with PTSD than other types of trauma. Despite this variability, the symptom expression of PTSD remains fairly consistent regardless of the type of trauma experienced.

Little is known regarding the prevalence of ASD and the adjustment disorders in the general population. Large-scale epidemiological studies, such as the World Health Organization (WHO) Mental Health Epidemiologic Survey, the Epidemiologic Catchment Area study, and the National Comorbidity Survey Replication, did not report on these disorders. Rates of ASD in community and clinical samples range from 7% to as high as 28% with a mean rate of 13% (Bryant et al., 2011), and rates of ASD are typically higher among victims of violent versus nonviolent traumas. When subsyndromal cases of ASD are included, estimates of the disorder increase from 10% to 32% with a mean rate of 23% (Bryant et al., 2011).

There are few reliable findings on the prevalence of adjustment disorders. This gap in knowledge is likely influenced by the poor delineation between adjustment disorders and normal or adaptive stress responses, as well as the use of adjustment disorders as a residual "last resort" diagnostic category in the *DSM-IV*. One epidemiological study, the European Outcome of Depression International Network, found a 1% prevalence of adjustment disorder with depressed mood (ODIN; Ayuso-Mateos et al., 2001). More circumscribed samples of adults suggest adjustment disorders are more common in hospital psychiatric consultation settings (12%; Strain et al., 1998; 18.5%; Foster & Oxman, 1994) and among psychiatric inpatient admissions (Koran et al., 2002). A recent meta-analysis found prevalence rates of 15.4% and 19.4% in palliative care and oncology settings, respectively (Mitchell et al., 2011).

PSYCHOLOGICAL AND BIOLOGICAL ASSESSMENT

There are a number of diagnostic measures for assessing PTSD.

Although revisions are underway, these measures reflect *DSM-IV*, rather than *DSM-5,* criteria for PTSD. The Clinician-Administered PTSD Scale (CAPS; Weathers, Keane, & Davidson, 2001) is the most common interviewer-based instrument for PTSD and has robust psychometric properties (Weathers et al., 2001). The CAPS includes a detailed assessment of each traumatic event, frequency and severity ratings for each symptom, and overall distress and impairment ratings. Several CAPS scoring algorithms have demonstrated good diagnostic utility (Weathers, Ruscio, & Keane, 1999). A common scoring method is to score a symptom as present if the frequency is greater than or equal to 1 and the intensity is greater than or equal to 2, and to further require the endorsement of a sufficient number of symptoms for each symptom cluster. This method favors sensitivity (0.91) over specificity (0.71), and thus may be better for screening purposes. Using a total dimensional cut-score of greater than or equal to 65, on the other hand, favors specificity (0.91) over sensitivity (0.82), and thus may be better for confirming a diagnosis (Weathers et al., 1999). Other interview measures include the PTSD Symptom Scale–Interview (PSS-I; Foa & Tolin, 2000) and the Structured Interview for PTSD (SI-PTSD; Davison, Smith, & Kudler, 1989).

Additionally, the Structured Clinical Interview for *DSM-IV* (SCID-IV; First, Spitzer, Gibbon, & Williams, 1996) and the Anxiety Disorders Interview Schedule (ADIS-IV; Brown, Di Nardo, & Barlow, 1994) contain a module for assessing the presence or absence of PTSD.

Self-report questionnaires may also be used to assess PTSD. Commonly used measures include the PTSD Checklist (Blanchard, Jones-Alexander, Buckley, & Forneris, 1996), the PTSD Symptom Scale–Self-Report (PSS-SR; Foa, Riggs, Dancu, & Rothbaum, 1993), and the Posttraumatic Diagnostic Scale (PDS; Foa, Cashman, Jaycox, & Perry, 1997). An extensive list of measures used to assess PTSD is available from the National Center for PTSD (www.ptsd.va.gov). As already noted, these measures are being revised to reflect recent changes to the diagnostic criteria of PTSD in *DSM-5*.

Aside from interview and self-report measures of PTSD, several physiological variables have been found to distinguish current PTSD from lifetime PTSD and the absence of PTSD. These include an increased resting heart rate, an increased response to non-trauma-related stressors, and increased heart rate, skin conductance, and diastolic blood pressure in response to trauma cues (Pole, 2007). However, the diagnostic utility of these physiological variables is limited in that they tend to be less accurate in predicting PTSD than interview-based and self-report assessments.

There are few empirically validated diagnostic measures for ASD or adjustment disorders. Measures designed specifically for ASD include the Acute Stress Disorder Interview and the Acute Stress Disorder Scale, both developed by the same group of investigators (ASDI, ASDS; Bryant, Harvey, Dang, Sackville, & Basten, 1998). The SCID-IV contains an optional module for ASD, as well as a section on adjustment disorders that specifies the diagnosis should not be made if the criteria for any other psychiatric disorders are met (First et al., 1996). With regard to physiological measures, there are some data indicating that individuals who subsequently develop PTSD have higher heart and respiration rates immediately post-trauma relative to those who do not (Bryant et al., 2011). However, these data are not limited to individuals with ASD, and are likely hampered by the same classification precision of these measures for PTSD.

ETIOLOGICAL CONSIDERATIONS

A number of causal mechanisms have been implicated in the development of PTSD. These include genetic factors, brain structure and neurochemical abnormalities, pre- and post-trauma life events, cognitive appraisals and attentional biases, and sociodemographic variables such as gender.

Behavioral and Molecular Genetics

Among Vietnam era veterans, the risk of developing PTSD has been explained by (a) a genetic factor common to alcohol use and PTSD, (b) a genetic factor associated with PTSD but not with alcohol use, and (c) unique environmental effects (Xian et al., 2000). Yet another twin study of Vietnam era veterans found that the genetic factors that accounted for the relationship between combat exposure and PTSD also accounted for the relationship between combat exposure and alcohol use (McLeod et al., 2001).

Genetic factors contributed more to the relationship between combat exposure and PTSD as compared to environmental factors, whereas genetic and environmental factors contributed equally to the relationship between combat exposure and alcohol use. Interestingly, the genetic factors that account for the presence of PTSD may also influence exposure to certain types of traumatic events. Concordance of both interpersonal violence and PTSD is higher among monozygotic twins compared to dizygotic twins, whereas other types of trauma (i.e., natural disasters, motor vehicle accidents) are not accounted for by genetic factors (Stein, Jang, Taylor, Vernon, & Livesley, 2002).

In terms of specific genetic markers, the 5-HTTLPR polymorphism has been associated with an increased risk of developing PTSD in specific groups of trauma survivors including hurricane survivors with a high degree of exposure (Kilpatrick et al., 2003) and individuals reporting a traumatic event in childhood as well as adulthood (Xie et al., 2009). A similar interaction has been reported for variants of polymorphisms in the FK506 binding protein 5 (FKBP5) gene, which is involved in regulating the intracellular effects of cortisol. Individuals with these variants, who reported severe child abuse, were found to be at increased risk for developing PTSD after experiencing a traumatic event in adulthood (Binder et al., 2008; Xie et al., 2009). This gene was underexpressed among survivors of the September 11, 2001 attacks on the World Trade Center who developed PTSD compared to those who did not (Yehuda et al., 2009). There is evidence for candidate genes in other systems (e.g., the dopamine system), but findings have been limited or inconsistent (Broekman, Olff, & Boer, 2007; Koenen, 2007; Nugent, Amstadter, & Koenen, 2008). Genetic research on the trauma and stress related disorders of the *DSM-5* are limited to PTSD.

NEUROANATOMY AND NEUROBIOLOGY

Several brain structures have been implicated in PTSD, including the amygdala, the medial prefrontal cortex, and the hippocampus. First, PTSD is associated with increased activation in the amygdala in response to trauma-related stimuli (Francati, Vermetten, & Bremner, 2007). This increased activity likely represents the neural substrates of exaggerated fear acquisition and expression and may explain the salience of trauma memories in PTSD (Rauch, Shin, & Phelps, 2006). Importantly, hyperactivity in the amygdala is not unique to PTSD; increased activity in response to disorder-related stimuli has also been noted in specific phobia and social anxiety disorder (Etkin & Wagner, 2007; Shin & Liberzon, 2010). Second, PTSD is associated with deficient functioning in the medial prefrontal cortex (Francati et al., 2007; Shin & Liberzon, 2010). This deficiency is thought to underlie inadequate top-down modulation of the amygdala (Rauch et al., 2006). Moreover, the medial prefrontal cortex is thought to regulate processes that are important for habituation and extinction of fear responses, including emotional appraisal (Liberzon & Sripada, 2008). Third, PTSD is associated with abnormalities in the hippocampus. These abnormalities may underlie difficulties contextualizing memories (e.g., recognizing that certain contexts are safe; Liberzon & Spirada, 2008; Rauch et al., 2006). A meta-analysis concluded that increased PTSD severity is associated with decreased volume of the hippocampus, as well as decreased volume in the amygdala and the anterior cingulate, a structure in the medial prefrontal cortex (Karl et al., 2006).

Decreased hippocampal volume likely represents a risk factor for developing PTSD, as opposed to a neurobiological effect of trauma (McNally, 2003). Consistent with this, hippocampal volume does not change over time following trauma exposure (Bonne et al., 2001). Moreover, a study of veteran twin pairs discordant for combat exposure and PTSD found that PTSD severity among affected twins was negatively correlated with not only their own hippocampal volume but also that of their nonexposed twin (Gilbertson et al., 2002).

The neurochemical underpinnings of PTSD likely involve catecholamines (epinephrine, norepinephrine, and dopamine) and cortisol, a hormone involved in the neuroendocrine response to stress, as well as a variety of other neurotransmitters (Yehuda, 2006). PTSD may also be characterized by disturbance of the hypothalamic-pituitary-adrenal axis, arising primarily from hypersensitivity of glucocorticoid (i.e., cortisol) receptors (Yehuda et al., 2009). This may represent a risk factor, although the research findings are not yet clearly integrated into a cohesive model.

There are few data specifically reporting on neurobiological models of ASD or adjustment disorders. When viewed as a stress reaction conceptually related to PTSD, ASD in particular may also involve a dysregulation of the neurotransmitter and neuroendocrine systems implicated in PTSD. Quite possibly as well, ASD may involve deficits in certain brain regions such as the hippocampus, which are implicated as a risk factor for PTSD.

Learning, Modeling, and Life Events

Clearly, traumatic life events contribute to PTSD. Less clear is whether trauma exposure and PTSD share a dose-response relationship in which frequency and/or intensity of trauma correspond with symptom severity. Rates of PTSD vary based on the type of traumatic event, with assaultive violence and sexual assault being associated with the highest rates (Breslau et al., 1998; Norris, 1992). Furthermore, rates of PTSD among Vietnam era veterans roughly correspond to degree of combat exposure (Dohrenwend et al., 2006). However, PTSD severity has not been found to correspond to severity of exposure in other trauma samples such as motor vehicle accident survivors and political prisoners (Başoğlu et al., 1994; Schnyder, Moergeli, Klaghofer, & Buddeberg, 2001). Importantly, a dose-response relationship between trauma exposure and PTSD may be nonlinear. That is, after a certain degree of trauma exposure, symptom exacerbation may reach a plateau (McNally, 2003).

PTSD may also be related to degree of trauma exposure prior to the traumatic event. Exposure to childhood physical or sexual abuse is associated with an increased risk of future trauma exposure, as well as the development of PTSD in response to those subsequent traumas (Koenen, Moffitt, Poulton, Martin, & Caspi, 2007). In addition to previous childhood abuse or neglect, meta-analyses on the topic have identified other pre-trauma risk factors for PTSD, such as level of prior psychological adjustment and/or the presence of a previous personal or family history of psychiatric illness. Post-trauma risk factors include a lack of social support and additional life stressors (Brewin, Andrews, & Valentine, 2000; Keane, Marshall, & Taft, 2006; Ozer, Best, Lipsey, & Weiss, 2008).

Few studies have examined risk factors specifically in relation to the development ASD or adjustment disorders. However, given the conceptual overlap between PTSD and ASD, they likely share similar pre- and post-trauma risk factors. Supporting this line of reasoning, one study found that individuals with a previous history of trauma exposure or PTSD and those with more psychiatric dysfunction were at greater risk for developing ASD when experiencing a new trauma (Barton, Blanchard, & Hickling, 1996). Specific to adjustment disorders, there is some indication of a greater risk of the disorder among individuals from disadvantaged backgrounds, but virtually no systematic data on the topic (APA, 1994).

Cognitive Influences

Cognitive influences of PTSD include maladaptive beliefs that one holds about the meaning of the traumatic event that is experienced (e.g., self-blame, guilt). Consistent with this view, cognitive processing therapy (CPT) emphasizes the importance of identifying and revising maladaptive beliefs about the trauma and promoting a more balanced integration of the traumatic event (Resick & Schnicke, 1993). Other possible cognitive mechanisms of PTSD include attentional or memory related biases toward threat-related stimuli or trauma-related material, which may specifically reflect a cognitive vulnerability to developing PTSD (Brewin & Homes, 2003; Thrasher & Dalgleish, 1999; Weber, 2008). PTSD may also be influenced by perceived seriousness of threat, which in turn may be influenced by cognitive variables such as poor contextualization of autobiographical memory (Ehlers & Clark, 2000). Although not specific to ASD, a number of studies have found that maladaptive or negative appraisals and beliefs predict the subsequent development of PTSD (Bryant, Salmon, Sinclair, & Davidson, 2007; Mayou, Bryant, & Ehlers, 2001).

Sex and Racial-Ethnic Considerations

Epidemiological surveys suggest that women are more likely to report sexual assault or child molestation and men are more likely to report physical assault, combat exposure, or being threatened or attacked with a weapon (Norris et al., 1992). Prevalence studies of PTSD further indicate that women are more likely to develop PTSD relative to men (at a 2:1 ratio) given exposure to a traumatic event (Norris et al., 2002). That is, women have a higher conditional risk of developing PTSD relative to men. Traumas associated with ASD are similar to those for PTSD. However, systematic efforts are needed to confirm whether gender differences in rates of ASD are comparable to those associated with PTSD.

Findings regarding the interplay between trauma exposure, PTSD, and race/ethnicity are often mixed (Pole, Gone, & Kulkarni, 2008). Overall, however, most studies have found comparable rates of PTSD between African Americans and Caucasians. The few studies that have found significant racial/ethnic differences report higher base rates of PTSD among African Americans relative to Caucasians that largely disappear once severity of trauma exposure is controlled for. The most consistent findings regarding PTSD and race/ethnicity pertain to Hispanics. Relative

to non-Hispanic Caucasians, Hispanics often have higher rates of PTSD in both community and clinical samples (Pole et al., 2008). Cultural context may influence some aspects of PTSD, but the disorder generally presents as a coherent group of symptoms across cultures. Parallel efforts to study the relationship between race/ethnicity in both ASD and adjustment disorders are lacking.

COURSE, PROGNOSIS, AND TREATMENT

According to the *DSM-5*, symptoms consistent with a diagnosis of PTSD may begin immediately following or long after a traumatic event, and there is sufficient evidence that PTSD can persist for several years after the index trauma. The diagnostic specifier "with delayed expression" allows for a diagnosis of PTSD when all of the criteria for the disorder are not met for 6 months or longer after the traumatic event. Although cases of delayed onset PTSD have been noted in the literature, these findings are likely due to an exacerbation of prior symptoms over time. Supporting this view, a review on the topic found that delayed-onset PTSD in the complete absence of prior symptoms was rare (Andrews, Brewin, Philpott, & Stewart, 2007), a conclusion that other empirical studies have since supported (Frueh, Grubaugh, Yeager, & Magruder, 2009).

Parallel with its theoretical underpinnings, clinical practice guidelines generally recommend cognitive behavioral interventions as the most effective treatment approach for PTSD (DVA, 2010; Foa, Keane, & Friedman, 2009; IOM, 2007; NICE, 2005). Treatments that fall under this umbrella typically include elements of psychoeducation, stress reduction, exposure to trauma-related cues and memories, and cognitive restructuring, with the latter two components being considered the "active ingredients" for PTSD symptom reduction.

Although there are a number of interventions that emphasize exposure and/or cognitive restructuring, the empirical data weigh heavily in support of two specific manualized treatments for adults with PTSD: Prolonged Exposure (PE; an exposure-based intervention; Foa, Hembree, & Rothbaum, 2007) and Cognitive Processing Therapy (CPT; predominantly a cognitive restructuring intervention that includes elements of exposure; Resick & Schnicke, 1993). The focus in PE is on habituation to graded fear exposures, whereas the focus in CPT is on modification of maladaptive trauma-related beliefs (e.g., denial or self-blame). However, CPT often includes exposure exercises, and PE often includes elements of cognitive restructuring. Adding cognitive restructuring to PE does not appear to increase its efficacy (Foa et al., 2005), nor does adding writing exposure exercises to CPT (Resick et al., 2008), indicating that the therapies are efficacious in both their combined and component forms. Reviews on the topic suggest the average patient receiving PE or CPT fares better than 86% to 90% of patients who are assigned to a control group (i.e., do not receive what is considered an active treatment) (Bradley, Greene, Russ, Dutra, & Westen, 2005; Powers, Halpern, Ferenschak, Gillihan, & Foa, 2010). Despite the overall efficacy of PTSD interventions, 18% to 35% of individuals who complete treatment retain the diagnosis at follow-up, with civilians showing dramatically greater improvement than military veterans (Bradley et al., 2005). Disability incentives to remain ill have been posited as one possible reason why veterans evidence less clinical improvement than civilians (Frueh, Grubaugh, Elhai, & Buckley, 2007), as have other characteristics unique to veteran

populations (e.g., nature of combat trauma). Additionally, treatment dropout rates hover around 30% across clinical populations (Cloitre, 2009).

Reflecting neurobiological models of the disorder, pharmacological treatments for PTSD act primarily on the neurotransmitters associated with fear and anxiety, which include serotonin, norepinephrine, GABA, and dopamine. Selective serotonin reuptake inhibitors (SSRIs) are generally considered the pharmacological treatment of choice for PTSD (DVA, 2010; Stein, Ipser, & McAnda, 2009), and this class of drugs include the only two medications that are currently FDA approved for the treatment of PTSD—sertraline (Zoloft) and paroxetine (Paxil). Although there is some support for the efficacy of psychotropic medications for the treatment of PTSD, not all practice guidelines support their use. For example, after a review of 37 PTSD pharmacotherapy trials, the Institute of Medicine determined that there was insufficient evidence in support of any psychotropic medications for PTSD including SSRIs (IOM, 2007). Additionally, psychotropic medications do not typically alleviate all the symptoms associated with this disorder and it is generally recommended that patients take medications in conjunction with a psychotherapy specifically developed to treat PTSD, particularly with more complex symptom presentations.

Brief cognitive behavioral interventions immediately posttrauma have yielded promising results in terms of preventing the subsequent development of PTSD among those with ASD (Bryant, Sackville, Dang, Moulds, & Guthrie, 1999; Bryant, Moulds, Nixon, & Basten, 2003; Echeburua, deCorral, Sarasua, & Zubizarreta, 1996; Gidron et al., 2001). These interventions generally consist of education about symptoms, relaxation training, exposure exercises, and cognitive therapy. In contrast, psychological debriefing interventions, which were sometimes used in the aftermath of traumatic events like natural disasters, have failed to demonstrate sufficient efficacy and are generally contraindicated with more severe traumas or posttraumatic reactions (Forneris et al., 2013; North & Pfefferbaum, 2013).

Due to the acute nature of most adjustment disorders, they often do not require treatment or require limited treatment. Additionally, however, the high degree of variability in the symptom expression of adjustment disorders has likely complicated the development of standardized treatment approaches. Consistent with this, systematic investigations on the efficacy of specific interventions for adjustment disorders are limited to two randomized controlled trials, one targeting adjustment disorder with depressed mood secondary to myocardial infarction (Gonzales-Jaimes & Turnbull-Plaza, 2003) and another targeting adjustment disorder resulting in occupational dysfunction (van der Klink, Blonk, Schene, & van Dijk, 2003). Both of these interventions were tailored for a specific target population and anticipated deficits, with the first demonstrating efficacy of the intervention in terms of symptom reduction and the latter in terms of decreasing absenteeism but not symptom reduction. Pharmacotherapy trials for the treatment of adjustment disorders are likewise few in number and have not established the superiority of antidepressants versus placebo for symptom reduction (Casey, 2009; Casey, Pillay, Wilson, et al., 2013). Less systematic efforts and clinical wisdom would suggest that psychosocial treatments for adjustment disorders should be relatively brief in duration and focus on decreasing or removing the stressor as well as improving the patients adaptation and coping skills.

IMPLICATIONS OF THE *DSM-5*

The development of a trauma and stress-related chapter in the *DSM-5* will help emphasize PTSD, ASD, and adjustment disorders as stress responses along a continuum that are clearly linked to an antecedent event. It is unlikely that prevalence rates of PTSD or ASD will change significantly as a result of changes made to their diagnostic criteria in *DSM-5.* However, the decreased emphasis in the *DSM-5* on dissociation symptoms for ASD will likely improve the disorder's ability to predict the subsequent development of PTSD. Refinements to the diagnostic criteria of adjustment disorders and its placement in a chapter with other stress reactions, rather than a residual diagnostic category, may increase providers' use of the diagnosis in clinical practice. Additionally, it may encourage more systematic research on adjustment disorders, both as an independent diagnosis and in relation to PTSD and ASD.

CASE STUDIES

Paul is a 26-year-old African American Iraq War veteran who presented to his local VA primary care clinic due to feelings of anxiety. Paul served two tours of duty in Iraq and witnessed multiple roadside bombings in which members of his unit were injured and killed. His final tour ended 2 years ago. He reports symptoms that began shortly after the first roadside bombing he witnessed while overseas and an increase in the severity and frequency of these symptoms since his return to the U.S. He experiences frequent nightmares and intrusive memories about Iraq, including nightmares and unwanted thoughts related to a bombing in which he witnessed the death of two of his comrades with whom he was particularly close. Paul questions in his mind why he lived while his comrades died and feels certain that he should have been able to prevent what happened. He avoids internal and external reminders of the event, which include thinking about the bombings and other graphic scenes from his service, as well as driving. Last, he is experiencing marked irritability, anger, and hypervigilance, especially while driving. Paul often catches himself gripping the steering wheel of his car, anticipating an intermittent explosive device. Because of his symptoms, Paul's relationships have suffered, most notably his relationship with his girlfriend of several years who has made a number of comments to him that he has changed since coming back from Iraq and is not the same "easygoing" guy she met. Paul is enrolled in college under the GI Bill and is having difficulty studying due to problems concentrating and a persistent lack of sleep. He fears he may have to withdraw from the semester.

Paul's experiences in Iraq are consistent with the definition of a traumatic event, and his symptoms reflect chronic PTSD with acute onset.

Claudia is a 45-year-old Hispanic woman who presented to her primary-care physician for her annual appointment. During the course of the appointment, Claudia admitted to her physician that she has been struggling emotionally since her recent divorce (9 months prior) and her son leaving for college (2 months prior). Since both of these events, but to a much greater extent since her son moved out of the home, Claudia describes feeling a mixture of depression and sadness about her failure as a wife, her loneliness since her son's departure, as well as general feelings of anxiety and fear about her future. She reports feeling at a loss as to how to manage her time and

feels overwhelming sadness at being 45 and alone, with few friends or family to rely on. She acknowledged calling in sick from work a few times a month for the past few months and then ruminating about the potential consequences of having not gone in to work. She reports watching television several hours a day followed by periods of anxious and somewhat obsessive housecleaning. She also reports having crying spells "over just about anything" and was tearful while discussing her symptoms during her primary-care appointment.

Claudia's clinical presentation is consistent with a diagnosis of adjustment disorder with mixed anxiety and depressed mood.

SUMMARY

PTSD, ASD, and adjustment disorders are classified in the *DSM-5* as trauma- and stress-related disorders that were precipitated by a stressful or traumatic event. The value of classifying these disorders together will enable clinicians to better differentiate normal and mild stress reactions from more severe and pathological stress reactions. It also more clearly highlights the temporal and symptom requirement distinctions between PTSD, ASD, and adjustment disorders. Whereas PTSD and ASD emphasize fear and anxiety responses, adjustment disorder symptoms can accommodate a broader range of stress reactions. Second, although there is an explicit potential for ASD to predict subsequent impairment (i.e., to predict PTSD), an adjustment disorder is typically viewed as a discrete disorder that has a fairly immediate and time limited symptom duration. A third distinction between PTSD, ASD, and adjustment disorders regards the timing of diagnosis. Adjustment disorders can be diagnosed immediately after the event, ASD can be diagnosed from two days to up to one month after the event, and PTSD can be diagnosed from one month to several years after the trauma.

In conclusion, based on being linked to a clear precipitating stressful or traumatic event, PTSD, ASD, and adjustment disorders are viewed as stress reactions along a continuum that are differentiated by the severity of the initial stressor, an anxiety focused or broader set of symptoms in reaction to the event, and the onset and duration of the symptoms. PTSD and ASD share many of the same symptoms, with ASD being limited in duration to one month, and in some but not all cases predicting the subsequent development of PTSD. The relationship between adjustment disorders, PTSD, and ASD is poorly understood as there has been little systematic study on the topic. The placement of adjustment disorders in the same chapter as PTSD and ASD in the *DSM-5* will likely prompt a better understanding of the unique and overlapping features of these disorders in relation to PTSD and ASD. Future studies will likely shed light on the similarities and differences between these three disorders with regard to prevalence, diagnosis, clinical presentation, correlates, and treatment.

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CHAPTER 11

Dissociative Disorders

STEVEN JAY LYNN, JOANNA M. BERG, SCOTT O. LILIENFELD,
HARALD MERCKELBACH, TIMO GIESBRECHT,
MICHELLE ACCARDI, and COLLEEN CLEERE

"The most recent edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5;* American Psychiatric Association [APA], 2013) defines dissociative disorders as conditions marked by a disruption of and/or discontinuity in the normal integration of consciousness, memory, identity, emotion, perception, body representation, motor control, and behavior" (p. 291). The presentation of dissociative disorders is often dramatic, perplexing, and highly variable, both within and across individuals. The hallmarks of dissociation are profound and often unpredictable shifts in consciousness, the sense of self, and perceptions of the environment.

DSM-5 asserts that the dissociative disorders share a common feature: They are frequently manifested in the wake of trauma and are influenced by their proximity to trauma (p. 291). Later in the chapter, we contrast the posttraumatic theory that is firmly embedded in the *DSM-5* account of dissociation with a competing theory that does not conceptualize trauma as a necessary precursor to dissociation. In the course of our discussion, we will present a case study that illustrates the treatment of a patient with dissociative identity disorder (DID) and highlight controversies that have dogged the field of dissociation since the time of Janet's seminal writings on the topic (1889/1973).

The *DSM-5* (APA, 2013) identifies three major dissociative disorders that we discuss in turn—dissociative amnesia, depersonalization/derealization, and dissociative identity disorder. We then present an overview of dissociation in general, followed by a more detailed discussion of diagnostic considerations, prevalence, assessment, and etiology specific to each of the dissociative disorders.

1. *Dissociative amnesia* is marked by an inability to recall important autobiographical information, usually of a traumatic or stressful nature inconsistent with ordinary forgetting. This condition most often "consists of localized or selective amnesia for a specific event or events, or generalized amnesia for identity and life history" (APA, 2013, p. 298).

2. *Depersonalization/derealization disorder (DDD)*, formerly known as depersonalization disorder, is diagnosed on the basis of symptoms of persistent depersonalization, derealization, or both. Depersonalization symptoms include experiences of unreality; feelings of detachment or being an outside observer of one's thoughts, feelings, sensations, or actions; an unreal or absent sense of self; physical and emotional numbing; and time distortion. In contrast, derealization experiences involve feelings of unreality or detachment with respect to one's surroundings that include the experience of individuals or objects as unreal, dreamlike, foggy, visually distorted, or lifeless.
3. *Dissociative identity disorder* (DID; formerly called multiple personality disorder) is marked by a disruption of identity characterized by two or more distinct personality states and recurrent gaps in the recall of everyday events, personal information, and/or traumatic events that are inconsistent with ordinary forgetting (APA, 2013, p. 292).

DSM-5 also includes a fourth category of other specified dissociative disorder, which does not meet full criteria for any dissociative disorder and includes chronic and recurrent syndromes of mixed dissociative symptoms, identity disturbance due to prolonged and intense coercive persuasion, acute dissociative reactions to stressors, and dissociative trance. Additionally, *DSM-5* includes a fifth category of unspecified dissociative disorder in which criteria are not met for a specific dissociative disorder and there is insufficient information to make a more specific diagnosis. Finally, *DSM-5* currently describes a dissociative subtype of posttraumatic stress disorder in which persistent or recurring feelings of depersonalization and/or derealization are manifested in reaction to trauma-related stimuli. *DSM-5* requires that the symptoms of all dissociative disorders must cause significant distress, impairment of functioning in major aspects of daily life, or both, and must not be attributable to the effects of a substance or another medical condition.

Some epidemiological studies among psychiatric inpatients and outpatients have reported prevalence rates of dissociative disorders exceeding 10% (Ross, Anderson, Fleischer, & Norton, 1991; Sar, Tutkun, Alyanak, Bakim, & Barai, 2000; Tutkun, Sar, Yargiç, Özpulat, Yank, & Kiziltan, 1998), and a study among community women in Turkey even reported a prevalence rate of 18.3% for lifetime diagnoses of a dissociative disorder (Sar, Akyüz, & Dogan, 2007). In contrast, many authors would take issue with these high prevalence rates in both clinical and nonclinical samples. Indeed, as our discussion will reveal, estimates of the prevalence of dissociative disorders vary widely and are associated with considerable controversy.

Although many authors regard symptoms of depersonalization/derealization and dissociative amnesia as core features of dissociation, the concept of dissociation is semantically open and lacks a precise and generally accepted definition (Giesbrecht, Lynn, Lilienfeld, & Merckelbach, 2008). This definitional ambiguity is related, in no small measure, to the substantial diversity of experiences that fall under the rubric of "dissociation." Dissociative symptoms range in their manifestation from common cognitive failures (e.g., lapses in attention), to nonpathological absorption and daydreaming, to more pathological manifestations of dissociation, as represented by the dissociative disorders (Holmes et al., 2005).

This variability raises the possibility that some of these symptoms are milder manifestations of the same etiology or have different etiologies and biological substrates, raising questions about whether dissociation is a unitary conceptual domain (Hacking, 1995; Holmes et al., 2005; Jureidini, 2003). Indeed, van der Hart and his colleagues (van der Hart, Nijenhuis, Steele, & Brown, 2004, 2006) have distinguished ostensibly trauma-related or pathological dissociation, which they term structural dissociation of the personality, from nonpathological dissociative experiences (e.g., altered sense of time, absorption). Structural dissociation, in turn, can be subdivided into levels that encompass primary dissociation, which is thought to involve one purportedly apparently normal part of the personality (ANP) and one emotional part of the personality (EP), secondary structural dissociation, supposedly associated with a single ANP and further division of the EP, and tertiary dissociation, ostensibly limited to DID and characterized by several ANPs and EPs. Nevertheless, as our review will demonstrate, researchers' attempts to discriminate pathological from nonpathological dissociative experiences psychometrically have been subject to criticism and have been less than uniformly successful (Giesbrecht, Lynn, Lilienfeld, & Merckelbach, 2008; Modestin & Erni, 2004; Waller, Putnam, & Carlson, 1996; Waller & Ross, 1997).

Other researchers (Allen, 2001; Cardeña, 1994; Holmes et al., 2005) have proposed two distinct forms of dissociation: detachment and compartmentalization. Detachment consists of depersonalization and derealization, which we describe in some detail later, and related phenomena, like out-of-body experiences. Psychopathological conditions that reflect symptoms of detachment include depersonalization disorder and feelings of detachment that occur during flashbacks in posttraumatic stress disorder (PTSD). Compartmentalization, in contrast, ostensibly encompasses dissociative amnesia, marked by extensive forgetting of autobiographical material, and somatoform dissociation, such as sensory loss and "unexplained" neurological symptoms (Nijenhuis, Spinhoven, Van Dyck, Van der Hart, & Vanderlinden, 1998). The core feature of compartmentalization is a deficit in deliberate control of processes or actions that would normally be amenable to control, as is evident in DID or somatization disorder. Although clinicians may find it helpful to subdivide dissociative symptoms into different symptom clusters (Bernstein-Carlson & Putnam, 1993), attempts to differentiate such clusters on a psychometric basis have not been consistently successful.

Dissociation is often presumed to reflect a splitting of consciousness, although it must be distinguished from the superficially similar but much debated concept of Freudian repression. Specifically, dissociation can be described as a "horizontal" split; that is, consciousness is split in two or more parts that operate in parallel. In contrast, repression is more akin to a "vertical" split, in which consciousness is arranged in levels, and traumatic or otherwise undesirable memories are ostensibly pushed downwards and rendered more or less inaccessible.

Although the existence of dissociation as a clinical symptom is not much in dispute, dissociative disorders are among the most controversial psychiatric diagnoses. Disagreement generally centers on the etiology of these disorders, with advocates often arguing for largely trauma-based origins (e.g., Dalenberg et al., 2012; Gleaves, 1996). In this light, dissociative symptoms are regarded as manifestations of a coping mechanism that serves to mitigate the impact of highly aversive or traumatic events (Gershuny & Thayer, 1999; Nijenhuis, van der Hart, & Steel, 2010). In contrast, skeptics

often emphasize the role of social influences, including cultural expectancies and inadvertent therapist cueing of symptoms (e.g., Lilienfeld et al., 1999; Lynn et al., in press; McHugh, 2008). As we will learn later in the chapter, the controversies stemming from etiology and classification of dissociative disorders extend to their assessment and treatment. We will focus our discussion on chronic dissociative symptoms, rather than dissociation at the time of a highly aversive event (i.e., peritraumatic dissociation). Also, we will not elaborate on the dissociative subtype of PTSD described in *DSM-5*. However, we will present a number of "state" measures of dissociation because researchers not infrequently consider temporary changes in dissociation in the context of research on more chronic presentations of dissociation.

DISSOCIATIVE AMNESIA

The diagnosis of dissociative amnesia requires that the memory loss is extensive and not attributable to substance use or to a neurological or other medical condition such as age-related cognitive loss, complex partial seizures, or closed-head brain injury and that the symptoms are not better explained by DID, PTSD, acute stress disorder, somatic symptom disorder, or major or mild neurocognitive disorder (APA, 2013, p. 298). This disorder, formerly referred to as psychogenic amnesia, often presents as retrospective amnesia for some period or series of periods in a person's life, frequently involving a traumatic experience.

DSM-5 lists several subtypes of dissociative amnesia. In localized amnesia, the individual cannot recall any information from a specific period of time, such as total forgetting of a holiday week. Selective amnesia involves the loss of memories for some, but not all, events from a specific period of time. In generalized amnesia, individuals cannot recall anything about their entire lives, and in continuous amnesia, individuals forget each new event as it occurs. Finally, systematized amnesia consists of the "loss of memory for specific categories of information" (e.g., sexual abuse, a particular person). These last three types of dissociative amnesia—generalized, continuous, and systematized—are much less common than the others, and may be manifestations of more complex dissociative disorders, such as DID rather than dissociative amnesia alone.

Lynn et al. (2014) argued that the central diagnostic criterion for dissociative amnesia is vague and subjective in stipulating that one or more episodes of inability to recall important information must be ". . . inconsistent with ordinary forgetting" (Dahlenberg et al., p. 522). The reliability of judgments of what constitutes "ordinary forgetfulness" is questionable, and what is "ordinary" hinges on a variety of factors, including the situational context and presence of comorbid conditions. A similar point was raised by Read and Lindsay (2000), who demonstrated that when people are encouraged to remember more about a selected target event, they report their forgetting to be more extensive, compared with individuals who are asked to simply reminisce about a target event.

Epidemiology

Because rates of reporting vary so widely, it is difficult to obtain reliable epidemiological information regarding dissociative amnesia. Questions concerning the validity

of dissociative amnesia as a diagnostic entity are supported by markedly different prevalence rates in the general population across cultures: 0.2% in China, 0.9% and 7.3% in Turkey, and 3.0% in Canada (Dell, 2009). These varying prevalence estimates could reflect genuine cultural differences, but they could just as plausibly reflect different interviewer criteria for evaluating amnesia.

The *DSM-5* states that dissociative amnesia can present in any age group, although it is more difficult to diagnose in younger children due to their difficulty in answering questions about periods of forgetting and possible confusion with a number of other disorders and conditions, including inattention, anxiety, oppositional behavior, and learning disorders. There may be just one episode of amnesia, or there may be multiple episodes, with each episode lasting anywhere from minutes to decades. Other sources (e.g., Coons, 1998) suggest that most cases occur in individuals in their 30s or 40s, and that 75% of cases last between 24 hours and 5 days. The prevalence of dissociative amnesia is approximately equal between genders. Still others argue that the scientific evidence for the existence of dissociative amnesia is unconvincing, and that barring brain injury or substance abuse or dependence, individuals who have experienced trauma do not forget those events (e.g., McNally, 2003; Pope, Hudson, Bodkin, & Oliva, 1998).

Certain cases of purported traumatic amnesia are in fact attributable to organic or other nondissociative causes. For example, when critiquing a "convincing demonstration of dissociative amnesia" (Brown, Scheflin, & Hammond, 1997), McNally (2004) discussed a study (Dollinger, 1985) of two children who witnessed a playmate struck and killed by lightning, and who were later diagnosed with dissociative amnesia. Yet as McNally noted, this diagnosis was clearly mistaken, because the children had also been struck by lightning and knocked unconscious.

Amusingly, and perhaps tellingly, Pope, Poliakoff, Parker, Boynes, and Hudson (2007) offered a reward of $1,000 to "the first individual who could find a case of dissociative amnesia for a traumatic event in any fictional or non-fictional work before 1800" (p. 225) on the basis that, whereas the vast majority of psychological symptoms can be found in literature or records dating back centuries, dissociative amnesia appears only in more modern literature beginning in the late 1800s. Over 100 individuals came forward with examples, but none met the diagnostic criteria for the disorder (although the prize later went to someone who discovered a case of dissociative amnesia in a 1786 opera, *Nina*, by the French composer Nicholas Dalayrac). Although Pope and colleagues' challenge does not "prove" anything regarding the validity of the disorder, its relative scarcity, and apparently recent (perhaps post late 18th century) development, raise troubling questions about its existence as a natural category or entity.

A special form of dissociative amnesia is crime-related amnesia. Many perpetrators of violent crimes claim to experience great difficulty remembering the essential details of the crime they committed (Moskowitz, 2004). Memory loss for crime has been reported in 25%–40% of homicide cases and severe sex offenses. Nevertheless, skeptics believe that genuine dissociative amnesia in these cases is rare. They have pointed out that trauma victims (e.g., concentration camp survivors) almost never report dissociative amnesia (Merckelbach, Dekkers, Wessel, & Roefs, 2003). For example, Rivard, Dietz, Matell, and Widawski (2002) examined a large sample of police officers involved in critical shooting incidents and found no reports of amnesia.

Also, recent laboratory research shows that when participants encode information while in a "survival mode," this manipulation yields superior memory effects (Nairne & Pandeirada, 2008). This finding is difficult to reconcile with the idea of dissociative amnesia while committing a crime. Thus, it is likely that feigning underlies most claims of crime-related amnesia (Van Oorsouw & Merckelbach, 2010).

DISSOCIATIVE FUGUE

Dissociative fugue (previously called psychogenic fugue) is arguably the most controversial dissociative phenomenon after dissociative identity disorder. In *DSM-IV-TR,* dissociative fugue (i.e., short-lived reversible amnesia for personal identity, involving unplanned travel or wandering) was listed as a separate diagnosis. In *DSM-5*, dissociative fugue—defined therein as apparently purposeful travel or bewildered wandering associated with amnesia for identity or other important autobiographical information—is no longer diagnosed as a disorder in its own right, but is instead coded as a condition that can accompany dissociative amnesia. In a fugue ("fugue" has the same etymology as the word "fugitive") episode, amnesia for identity may be so extreme that a person physically escapes his or her present surroundings and adopts an entirely new identity. If and when this identity develops, it is often characterized by higher levels of extraversion than the individual displayed prefugue, and he or she usually presents as well integrated and nondisordered.

Periods of fugue vary considerably across individuals, both in duration and in distance traveled. In some cases, the travel can be a brief and relatively short trip, whereas, in more extreme cases, it can involve traveling thousands of miles and even crossing national borders. While in the dissociative fugue state, individuals often appear to be devoid of psychopathology; if they attract attention at all, it is usually because of amnesia or confusion about personal identity. Again, it is doubtful that fugues constitute a fixed and cross-cultural diagnostic category. Hacking (1995) provides a detailed historical and critical analysis of fugue showing that they first appeared in the 19th century and since that time fluctuated in apparent prevalence and acceptance by the psychiatric community.

DIAGNOSTIC CONSIDERATIONS

Although *DSM-5* notes that dissociative fugue, with travel, is not uncommon in DID, dissociative fugue may manifest with other symptoms, including depression, anxiety, dysphoria, grief, shame, guilt, stress, and aggressive or suicidal impulses (APA, 2013). Reportedly, the condition often develops as a result of traumatic or stressful events, which has led to controversy and ambiguity regarding the relation between dissociative fugue and PTSD. Precipitants associated with the development of dissociative fugue include war or natural disasters, as well as the avoidance of various stressors, such as marital discord or financial or legal problems (Coons, 1998). Such avoidance suggests that clinicians must be certain to rule out malingering and factitious disorders before diagnosing dissociative fugue.

Certain culture-bound syndromes exhibit similar symptoms to dissociative fugue. These include *amok*, present in Western Pacific cultures (which has given rise to the colloquialism "running amok"); *pibloktok*, present in native cultures of the Arctic, and

Navajo "frenzy" witchcraft, all of which are marked by "a sudden onset of a high level of activity, a trancelike state, potentially dangerous behavior in the form of running or fleeing, and ensuing exhaustion, sleep, and amnesia" for the duration of the episode (APA, 2000, p. 524; Simons & Hughes, 1985).

Epidemiology

DSM-IV-TR places the population prevalence estimate of dissociative fugue at .02%, with the majority of cases occurring in adults (APA, 2000, p. 524). Ross (2009b) observed that in the approximately 3,000 individuals he treated in his trauma program over a 12-year period, he encountered fewer than 10 individuals with pure dissociative amnesia or pure dissociative fugue, although he noted that symptoms of amnesia and fugue were common in the patients he admitted.

DEPERSONALIZATION/DEREALIZATION DISORDER

Depersonalization/derealization disorder (DDD) is one of the most common dissociative disorders and perhaps the least controversial. In DDD, reality testing remains intact (APA, 2013, p. 302): Individuals are aware that the sensations are not real and that they are not experiencing a break from reality akin to psychosis. In a departure from *DSM-IV,* in which depersonalization and derealization were diagnosed separately, *DSM-5* created a new diagnostic category of depersonalization/derealization disorder. This "lumping" of formerly separate conditions is supported by findings (Simeon, 2009a) that individuals with derealization symptoms do not differ significantly from those with depersonalization accompanied with derealization in salient respects (e.g., illness characteristics, comorbidity, demographics).

Greatly contributing to our knowledge about depersonalization symptoms has been the development of well-validated screening instruments, notably the Cambridge Depersonalization Scale (CDS; Sierra & Berrios, 2000; Sierra, Baker, Medford, & David, 2005). Depersonalization episodes are not uncommonly triggered by intense stress and are often associated with high levels of interpersonal impairment (Simeon et al., 1997). Episodes of depersonalization or derealization are also frequently associated with panic attacks, unfamiliar environments, perceived threatening social interactions, the ingestion of hallucinogens, depression, and PTSD (Simeon, Knutelska, Nelson, & Guralnik, 2003). Individuals with DDD are also more likely than healthy individuals to report a history of emotional abuse. In contrast, general dissociation scores are better predicted by a history of combined emotional and sexual abuse (Simeon, Guralnik, Schmeidler, Sirof, & Knutelska, 2001).

Diagnostic Considerations

Nearly 50% of adults have experienced at least one episode of depersonalization in their lifetimes, usually in adolescence, although a single episode is not sufficient to meet criteria for the disorder (Aderibigbe, Bloch, & Walker, 2001). Because depersonalization and derealization are common, DDD should be diagnosed only if these symptoms are persistent or recurrent and are severe enough to cause distress, impairment in functioning, or both. The distress associated with DDD may be

extreme, with sufferers reporting they feel robotic, unreal, and "unalive." They may fear becoming psychotic, losing control, and suffering permanent brain damage (Simeon, 2009a). Individuals with DDD may perceive an alteration in the size or shape of objects around them. Other people may appear mechanical or unfamiliar, and affected individuals may experience a disturbance in their sense of time (Simeon & Abugel, 2006).

A diagnosis of DDD requires that the symptoms do not occur exclusively in the course of another mental disorder, nor can they be attributable to substance abuse or dependence or to a general medical condition. Furthermore, DDD should not be diagnosed solely in the context of meditative or trance practices. Symptoms of other disorders, such as anxiety disorders, major/unipolar depression, and hypochondriasis and certain personality disorders, especially avoidant, borderline, and obsessive-compulsive, may also be present (Simeon et al., 1997). Depersonalization and derealization symptoms are often also part of the symptom picture of acute stress disorder (ASD; APA, 2013), which is often a precursor to PTSD.

EPIDEMIOLOGY

DSM-5 estimates the lifetime prevalence of DDD in the United States as 2%, with a range of 0.8% to 2.8% (see also Ross, 1991), suggesting that DDD might be as common as or more common than schizophrenia and bipolar disorder. DDD is diagnosed almost equally often in women as in men (Simeon et al., 2003). It frequently presents for treatment in adolescence or adulthood, even as late as the 40s, though its onset may be earlier. Estimates of the age of onset of DDD range from 16.1 (Simeon et al., 1997) to 22 years (Baker et al., 2003).

The onset and course of DDD vary widely across individuals. Some people experience a sudden onset and others a more gradual onset; some experience a chronic form of the disorder, whereas others experience it episodically. In about two-thirds of people with DDD, the course is chronic, and symptoms of depersonalization are present most of the time, if not continually. Episodes of depersonalization may last from hours to weeks or months, and in more extreme cases, years or decades (Simeon, 2009a).

DISSOCIATIVE IDENTITY DISORDER

According to *DSM-5*, "the defining feature of dissociative identity disorder is the presence of two or more distinct personality states or experiences of possession" (APA, 2013, p. 292). Thus, the requirement that people diagnosed with DID must experience distinct identities that recurrently take control over one's behavior is no longer present. Importantly, in *DSM-5* "distinct personality states" replaces the term *identities*. The diagnostic language in *DSM-5* represents a distinct departure from *DSM-II* (APA, 1968), which used the term multiple personalities, and from *DSM-IV* (APA, 1994), which labeled the condition dissociative identity disorder to underscore alterations in identity, rather than fixed and/or complete "personalities."

These shifts in diagnostic criteria may prove to be problematic and result in changes in the prevalence rates of DID. For example, what constitutes a personality state or an experience of possession may be open to greater interpretation compared with

previous iterations of *DSM*. Moreover, in *DSM-5*, signs and symptoms of personality alteration may be not merely "observed by others," but also "reported by the individual" (APA, 2013; p. 292), further expanding opportunities for the diagnosis of DID. In cases in which alternate personality states are not witnessed, in *DSM-5* it is still possible to diagnose the disorder when there are "sudden alterations or discontinuities in sense of self or agency . . . and recurrent dissociative amnesias" (APA, 2013; p. 293), creating even more latitude and subjectivity in the diagnosis of DID. Moreover, amnesia is no longer restricted to traumatic events and may now be diagnosed in relation to everyday events, which may also increase the base rates of diagnosed DID. Although *DSM-5* no longer defines DID in terms of "distinct identities that recurrently take control of the individual's behavior (*DSM-IV*, p. 519)," in the remainder of the chapter, we will not refrain from using the terms *personalities* and *identities*, insofar as these terms (a) continue to be widely used in the extant literature and (b) encompass "personality states."

Diagnostic Considerations

To meet diagnostic criteria for DID, an individual's symptoms cannot be attributable to substance use or to a medical condition, and the "disturbance is not a normal part of a broadly accepted cultural or religious practice" (APA, 2013; p. 292). When the disorder is assessed in children, the symptoms must not be confused with imaginary play. To recognize cultural variants of dissociative phenomena, *DSM-5* refers to a "possession form" of DID, which is "typically manifest as behaviors that appear as if a 'spirit,' supernatural being, or outside person has taken control, such that the individual begins speaking or acting in a distinctly different manner" (APA, 2013, p. 293). Because such manifestations are not uncommon in different cultures (see Cardeña, van Duijl, Weiner, & Terhune, 2009 for a discussion of trance/possession phenomena), to warrant a diagnosis of DID, the identities must be present recurrently, be unwanted or involuntary, engender significant distress or impairment, and not be a part of accepted cultural/religious practices.

In nonpossession forms of DID, there is typically considerable variation in the presentation of symptoms. Nevertheless, the primary identity or personality state in an individual with DID often carries the individual's given name and tends to be "passive, dependent, guilty, and depressed." Other personalities, often called "alters," may be assertive or even aggressive and hostile, and these more dominant identities usually possess more complete memories regarding the individual's actions and history. Within one individual, there can often be anywhere between 2 and 100 or more personalities, with approximately 50% of individuals reporting 10 or fewer distinct identities, although extreme cases of many as 4,500 alters have been reported (Acocella, 1999). Reported identities are usually just "regular" people, but more extreme and bizarre cases exist. There have been reports of identities claiming to be Mr. Spock from *Star Trek*, the rock star Madonna, the bride of Satan, and even a lobster.

Researchers have documented substantial comorbidity of DID with other disorders. For example, Ellason, Ross, and Fuchs (1996) reported that DID patients met criteria for an average of 8 Axis I disorders and 4.5 Axis II disorders. One-half to two-thirds of patients with DID meet diagnostic criteria for borderline personality disorder (BPD; Coons, Bowman, & Milstein, 1988; Horevitz & Braun, 1984). Conversely,

Sar, Akyuz, Kugu, Ozturk, and Ertem-Vehid (2006) found that 72.5% of patients screened for BPD had a dissociative disorder. In one study, researchers (Kemp, Gilbertson, & Torem, 1988) reported no significant differences between BPD and DID patients on measures of personality traits, cognitive and adaptive functioning, and clinician ratings, suggesting noteworthy commonalities between the two conditions. Histories of sexual and physical abuse are also commonly reported in both patient groups, and BPD patients score well above general population norms on measures of dissociation (Lauer, Black, & Keen, 1993). Indeed, Lauer and his colleagues (Lauer, Black, & Keen, 1993) suggested that DID is an epiphenomenon of the combination of BPD with high suggestibility.

Individuals with DID often experience additional symptoms, including self-mutilation; suicidal or aggressive behavior; as well as major depression; substance abuse; and sexual, eating, and sleep disorders (Fullerton et al., 2000; North, Ryall, Ricci, & Wetzel, 1993; Ross, 1997). Accordingly, some clinicians have argued that the DID diagnosis really is a severity marker identifying extreme variants of a host of other disorders (for an extensive discussion see North et al., 1993).

Many DID patients meet the criteria for schizoaffective disorder (Lauer et al., 1993), and as many as half have received a previous diagnosis of schizophrenia (Ross & Norton, 1988). Indeed, auditory and visual hallucinations are common in both DID and schizophrenia. However, patients with DID commonly report that hallucinated voices originate inside of their heads, whereas patients with schizophrenia tend to perceive the origin of voices outside of their heads and possess less insight into the nature of their symptoms (Coons, 1998; Kluft, 1993).

DID patients have been reported to endorse more positive symptoms (e.g., delusions, hallucinations, and suspiciousness) and Schneiderian first-rank symptoms, which include themes of passivity, than schizophrenic patients (Ellason & Ross, 1995; Steinberg, Rounsaville, & Cichetti, 1990). Ellason and Ross (1995) argued that the presence of positive symptoms can be used to formulate an accurate differential diagnosis between the two disorders, although further research regarding this possibility is necessary (for further diagnostic considerations see Steinberg & Siegel, 2008).

PTSD is one of the most commonly comorbid conditions with DID (Loewenstein, 1991). Moreover, PTSD patients are more likely to present with symptoms of dissociation (e.g., numbing, amnesia, flashback phenomena) than patients with major depression, schizophrenia, and schizoaffective disorder (Bremner, Steinberg, Southwick, Johnson, & Charney, 1993).

EPIDEMIOLOGY

DID may be episodic or continuous, and in some cases may remit after the late 40s (APA, 2000). There are documented cases of DID extending decades, and the concept of fragmented or multiple personalities is an ancient one. That said, the number of cases has increased exponentially in the past few decades. Prior to 1970, there were approximately 80 reported cases, but by 1986 that number had ballooned to approximately 6,000. As of 1998, there were approximately 40,000 cases (Lilienfeld & Lynn, in press).

Population prevalence estimates vary widely, from extremely rare (e.g., Piper, 1997; Rifkin, Ghisalbert, Dimatou, Jin, & Sethi, 1998) to rates approximating that of

schizophrenia (1–2%; Coons, 1998; Ross, 1997). Estimates of DID in inpatient settings range from 1–9.6% (Rifkin et al., 1998; Ross, Duffy, & Ellason, 2002). In addition to the dramatic increase in DID's prevalence over the past few decades, there has been an increase in the number of "alters" reported, from only two or three separate identities to an average of approximately 16 (interestingly, the exact number reported by Sybil; see below) by 1990.

DID is between 3 and 9 times more common in women than men, and women also tend to have more identities (an average of 15, as compared with the male average of 8; APA, 2000). Nevertheless, this imbalanced sex ratio may be an artifact of selection and referral biases (Lynn, Fassler, Knox, & Lilienfeld, 2009). In particular, a larger proportion of males with DID may end up in prisons (or other forensic settings) than in clinical settings (Putnam & Loewenstein, 2000).

DID is the most controversial dissociative disorder, and easily among the most controversial disorders in *DSM-5*. Skeptics of the disorder (Paris, 2012; Piper & Merskey, 2004) argue that its proliferation is in part a function of media exposure. In 1976, the movie *Sybil* was released, documenting the real-life story of a woman who had supposedly experienced severe child abuse and later developed 16 personalities (but see "Etiological Considerations" section for evidence calling into question significant details of the Sybil case). In addition to the number of cases increasing after the release of this movie, the number of individuals reporting child abuse as a cause of DID also rose drastically (Lilienfeld & Lynn, in press; Spanos, 1996). In contrast, proponents of the disorder respond that clinicians now are simply better equipped to identify the disorder (Gleaves, May, & Cardena, 2001). We elaborate on this etiological debate later in the chapter.

PSYCHOLOGICAL ASSESSMENT

A variety of assessment instruments are available to evaluate dissociation and dissociative disorders. In this section, we review commonly used structured interview and self-report measures.

Structured Interview Measures

The Structured Clinical Interview for *DSM-IV* (SCID-D; Steinberg, 1985) and its revision (SCID-D-R; Steinberg, 1994) are semistructured interviews that systematically assess five core symptoms of dissociation: amnesia, depersonalization, derealization, identity confusion, and identity alteration. The SCID-D incorporates the *DSM-IV* criteria for dissociative disorders. The full 250-item administration may take 2–3 hours for psychiatric patients with dissociative symptoms; however, nondissociative psychiatric patients may complete the interview in 30 to 90 minutes, and nonpsychiatric participants in 30 minutes. The severity of each of the five core symptoms is scored in terms of distress, dysfunctionality, frequency, duration, and course. The revised scale was administered in NIMH field trials that encompassed 350 interviews of dissociative and nondissociative adults. Reports from the field trials (N = 141 mixed psychiatric patients) revealed that the interexaminer and temporal reliability of the SCID-D-R ranges from very good to excellent (weighted kappa 0.77–0.86) for both the presence and extent of dissociative symptoms over three time periods. For type of

dissociative disorder, interexaminer agreement ranged from 0.72–0.86, and test-retest reliability for the overall presence of a dissociative disorder was good (0.88 over 7-day period). The SCID-D-R possesses good convergent validity, and is capable of distinguishing DID patients from patients with anxiety disorders, substance abuse, personality disorders, eating disorders, and psychotic disorders (Cardena, 2008). The SCID-D may be helpful in discriminating DID from feigning. It also appears to distinguish DID from schizophrenia (Wellburn et al., 2003). Nevertheless, Kihlstrom (2005, p. 3) countered that "even with relatively strict criteria in place, it can be difficult to discriminate between dissociative disorders and bipolar disorder, borderline personality disorder, and even schizophrenia."

The Dissociative Disorders Interview Schedule (DDIS; Ross et al., 1989) is a structured interview used to assist in the diagnosis of dissociative disorders, as well as conditions that often co-occur with it, including somatization disorder, major depressive disorder, and borderline personality disorder. The interview has been used for clinical and research purposes and consists of 16 sections with a total of 131 questions. The interview is highly structured to minimize interviewer confirmation bias and sequenced so that indirect questions about secondary features of DID precede increasingly specific questions.

In the original validation study, 80 psychiatric patients from specialized research clinics were interviewed. Patients diagnosed with DID ($n = 20$) were compared with patients with panic disorder ($n = 20$), eating disorder ($n = 20$), and schizophrenia ($n = 20$). For DID, the DDIS yielded a sensitivity of 90% and a specificity of 100% [see also Ross et al. (1992) who demonstrated high agreement (94.1%) of DDIS classification using the DDIS with independent clinical evaluation]. The authors reported that interrater reliability was adequate ($r = .68$; Ross et al., 1989). The DDIS has demonstrated good convergent validity, as indexed by high correlations of DID diagnosis scores with the DES ($r = .67$–$.78$; Cardena, 2008). Nevertheless, the authors (Ross et al., 1989) cautioned that depersonalization disorder cannot be reliably diagnosed using the DDIS (interrater reliability = .56).

The Clinician Administered Dissociation State Scale (CADSS; Bremner et al., 1998) was developed to assess dissociative states. The clinician verbally administers 19 "subject-rated" items on a Likert-type scale ranging from 0 (not at all) to 4 (extremely). Three subscales subsume the subject-rated items: amnesia, depersonalization, and derealization. The clinician also observes the participant's behavior during the interview and rates eight behaviors presumed to indicate the presence of a dissociative state on the same Likert-type scale as the subject-rated items.

In the original study, the CADSS was administered to patients with combat-related PTSD and a comorbid dissociative disorder (PTSD/dissociative) ($n = 68$). These patients were compared with patients with schizophrenia ($n = 22$), mood disorders ($n = 15$), healthy controls ($n = 8$), and combat veterans without PTSD ($n = 11$). The CADSS discriminated between patients with PTSD and comorbid dissociative disorders (86% of cases) and patients with the comparison conditions. Furthermore, the CADSS detected changes in dissociative symptoms before and after patients with PTSD participated in a traumatic memories group. These patients showed a significant increase in symptoms compared with baseline, suggesting that the CADSS may be sensitive enough to capture changes in repeated measures designs. Interrater reliability was excellent for the total scale (ICC = .92) and for the

subject-rated portion (ICC = .99), but was markedly lower for the observer ratings (ICC = .34). The internal consistency of the CADSS was good to excellent for the total scale (α = .94), subjective portion (α = .94), observer ratings (α = .90), and the individual subscales (α = .74–.90). Recently, Condon and Lynn (in press) reported that the CADSS correlated at r =.63 with the DES-II and reported the internal consistency of the CADSS to be α = .80 in a sample of undergraduates.

Self-Report Measures

The Dissociative Experiences Scale (DES; Bernstein & Putnam, 1986) and its revision (DES-II; Bernstein-Carlson & Putnam, 1993) are brief self-report measures of dissociation that can be used in both research and clinical settings to assess individuals within normal and psychiatric populations. Participants rate 28 items pertaining to dissociation in terms of the frequency they are experienced, from 0% to 100%. In the original sample, the test-retest reliability among 192 participants was .84 over a period of 4 to 8 weeks, and split half reliability coefficients ranged from .71 to .96, indicating good internal consistency. In addition, DES scores differentiated participants with a dissociative disorder (e.g., DID) from those without a dissociative disorder (e.g., normal adults, late adolescent college students, alcoholics, phobics). A cutoff of 30 correctly identified 74% of patients with DID and 80% of subjects without DID in a multicenter study (Carlson, Putnam, Ross, Torem, et al., 1991).

The DES is the most frequently used self-report measure of dissociation (Brand, Armstrong, & Loewenstein, 2006). Nevertheless, researchers have questioned whether the scale is unidimensional, as would be expected of a factorially pure measure of dissociation. Carlson et al. (1991) reported a three-factor solution—amnesia, absorption (related to openness to experience), and depersonalization (also see Ross, Ellason, & Anderson, 1995; Sanders & Green, 1994)—and others (Ray & Faith, 1994) have identified four factors. In contrast, Waller (1995) reanalyzed Carlson et al.'s (1991) data and concluded that their three-factor solution could reflect the skewed distribution of the items, and thus might be a statistical artifact reflecting the presence of difficulty factors (that is, factors induced by similar levels of skewness across the items; see also Holmes et al., 2005; Wright & Loftus, 1999).

Waller, Putnam, and Carlson (1996) responded to criticisms that the DES contains a substantial number of nonpathological items that tap absorption (e.g., "Some people find that when they are watching television or a movie they become so absorbed in the story that they are unaware of other events happening around them.") by developing the DES-Taxon (DES-T) scale. This 8-item scale contains items from the original DES that measure pathological dissociation, including derealization, depersonalization, psychogenic amnesia, and identity alteration. Waller and Ross (1997) estimated that the general population base rate of pathological dissociation is 3.3%. Of course, being classified as a taxon member (i.e., distinct type or latent class) cannot be equated with DID (Modestin & Erni, 2004), as the prevalence of DID in the general population is almost certainly much lower than 3%. Although the resulting scale was stricter in the criteria for establishing evidence of pathologic dissociation, the data supporting its validity are mixed. Simeon and colleagues (Simeon et al., 1998) found that the DES-T sum score is superior to the standard DES at distinguishing patients with depersonalization disorders (DDD) from control subjects. Nevertheless, later studies

revealed that the DES-T: (a) classified only 64% of patients with DDD as having a dissociative disorder (Simeon et al., 2003), (b) produced high false positive rates (Giesbrecht, Merckelbach, & Geraerts, 2007), and (c) lacked temporal stability for taxon membership probability (Watson, 2003). Nevertheless, many studies have documented significant differences between people who score high versus low on both the DES and the DES-T with respect to a variety of measures of memory and cognition (Giesbrecht et al., 2008).

The Adolescent Dissociative Experiences Scale (A-DES; Armstrong, Putnam, Carlson, Libero, & Smith, 1997) is a 30-item self-report measure designed exclusively for use with adolescent populations. The scale is intended to serve as a screening tool for dissociative disorders among adolescents and trace the developmental trajectories of normal and pathological dissociation over time. The A-DES items are rated on an 11-point Likert-type scale, and comprise the following subscales: dissociative amnesia, absorption and imaginative involvement, passive influence, and depersonalization and derealization. The A-DES was normed using a group of healthy adolescents in junior-high and high school populations (Smith & Carlson, 1996) and a group of adolescent clinical patients (Armstrong et al., 1997). The authors reported excellent internal consistency for the total score (α = .93) and subscales (α = .72–85). Nevertheless, there are questions concerning the A-DES's convergent validity. In a sample of 331 nonreferred youths, Muris, Merckelbach, and Peeters (2003) reported that A-DES scores are not only significantly related to PTSD symptoms and fantasy proneness, but also to other anxiety symptoms.

The Multidimensional Inventory of Dissociation (MID 5.0; Dell, 2006) is a recently developed self-report measure created to assess the symptom-domain of DID and the phenomenological domain of dissociation. The MID 5.0 contains 168 dissociation items and 50 validity items rated on a 0–10 Likert-type scale. The MID shows promising convergent validity with other psychiatric diagnoses (e.g., it distinguishes among individuals with DID, dissociative disorder not otherwise specified, mixed psychiatric, and nonclinical adults; Dell, 2002) and self-report measures (e.g., correlations with the DES = .90; Dell, 2006), as well as structural validity (e.g., factor analyses isolated a single overarching factor of pathological dissociation; see Dell, 2006). Nevertheless, these findings have yet to be replicated by independent research groups. The author reported good-to-excellent internal consistency of the 23 dissociation scales (α = 0.84–0.96) and temporal stability (4- to 8-week test-retest interval; *r*s = .82–.97) in a large clinical sample. These latter results were replicated in Israel and Germany (see Dell, 2006).

The Somatoform Dissociation Questionnaire (SDQ-20; Nijenhuis, Spinhoven, Van Dyck, Van der Hart, & Vanderlinden, 1996) is a self-report measure designed to evaluate the presence of somatoform responses associated with dissociative states that cannot be medically explained. Participants rate items on a 5-point Likert-type scale. Twenty of the 75 original items discriminated outpatients with dissociative disorders from nondissociative psychiatric outpatients and comprised the final scale. The authors reported excellent internal consistency (α = 0.95) and higher scores among patients with DID compared with patients with dissociative disorder not otherwise specified. The authors also reduced the SDQ-20 to a five-item screen for dissociative disorders (SDQ-5; Nijenhuis, Spinhoven, Van Dyck, Van der Hart, & Vanderlinden, 1997). For dissociative disorders among psychiatric patients, the SDQ-5 exhibited a

sensitivity of 94% and a specificity of 98% (Nijenhuis et al., 1998). A study in which DES, MID, and SDQ-20 were compared to SCID-D outcomes in psychiatric outpatients found that these self-report instruments have comparable diagnostic accuracy and are equivalently suitable as screening tools for dissociative disorders (Mueller-Pfeiffer et al., 2013).

The Dissociation Questionnaire (DIS-Q; Vanderlinden, Van Dyck, Vandereycken, & Vertommen, 1991) was developed to account for sociocultural differences in European populations as well as to assess a broad spectrum of dissociative experiences. The authors generated items from existing dissociation questionnaires and clinical experience. Participants rate items on a 1–5 Likert-type scale; the final 63-item scale was normed on 374 participants from the general population in Belgium and the Netherlands. Four factors constitute the DIS-Q (i.e., identity confusion, loss of control, amnesia, and absorption). Internal consistency of the subscales ($\alpha = 0.67$–0.94) and the overall scale ($\alpha = 0.96$) were good to excellent, as was test-retest reliability over a period of 3–4 weeks. The authors report successful discrimination of patients with dissociative disorders and nondissociative disorders with the exception of PTSD. Within the dissociative disorders, the DIS-Q successfully discriminated DID from dissociative disorder–not otherwise specified.

The State Scale of Dissociation (SSD; Kruger & Mace, 2002) is a self-report inventory designed to detect changes in dissociative states, rather than traits. The SSD was developed using existing scales, the DSM-IV, and the ICD-10, along with the aid of clinical experts. The 56-item scale is scored on a Likert-type scale from 0–9 and broken down into seven subscales: derealization, depersonalization, identity confusion, identity alteration, conversion, amnesia, and hypermnesia (remembering things too well). In the original study, the SSD was administered to 130 patients with major depression ($n = 19$), schizophrenia ($n = 18$), alcohol withdrawal ($n = 20$), dissociative disorders ($n = 10$), and healthy controls ($n = 63$). A score of > 3.9 nearly doubled the certainty of a diagnosis of a dissociative disorder, although an important limitation is the small sample of dissociative patients. The internal consistency of the SSD was good to excellent for the total scale ($\alpha = 0.97$), and correlations between the SSD and the DES among people with a dissociative disorder were $r = .81$, and $r = .57$ in healthy controls. Following a brief grounding activity (53 minutes, during which participants completed a number of other scales), the SSD scores among all participants decreased significantly on retest, suggesting that the SSD is sensitive to short-term changes in dissociative states across diagnostic groups.

The *Cambridge Depersonalization Scale (CDS*; Sierra & Berrios, 2000) consists of 29 items that ask respondents to rate recent depersonalization symptoms on a 5-point frequency scale (anchors: 0 = never; 4 = all the time) and a 6-point duration scale (anchors: 1 = few seconds; 6 = more than a week). The scale differentiates patients with DDD from other patient groups (e.g., patients with epilepsy, anxiety disorders) and from healthy controls (Sierra & Berrios, 2000). Sierra and Berrios (2000, 2001) reported sound internal consistency for the CDS (e.g., $\alpha = 0.89$). An exploratory factor analysis identified four factors that accounted for 73.3% of the variance: anomalous body experience, emotional numbing, anomalous subjective recall, and alienation from surroundings (Sierra et al., 2005).

Assessment is often an ongoing process in psychotherapy, and much information can be gleaned in the absence of standardized tests of dissociative experiences and

symptoms. In this regard, a number of caveats are in order. Less formal assessment procedures that even subtly suggest a history of abuse or validate the manifestation of alters with separate histories (e.g., personality "system mapping" to establish contact with nonforthcoming alters, providing names to alters, prompting or suggesting the emergence appearance of alters) should be avoided. A concern is that therapists who repeatedly ask leading questions such as "Is it possible that there is another part of you with whom I haven't yet spoken?" may elicit via suggestion imagined-believed-in alter personalities that ostensibly account for their clients' otherwise enigmatic behaviors (e.g., self-mutilation, and rapid and intense mood shifts). Repeated questioning about historical events is not helpful, as it can lead patients to mistakenly believe that they have significant gaps (e.g., amnesia) in their autobiographical memories of childhood (Belli, Winkielman, Read, Schwartz, & Lynn, 1998; Read & Lindsay, 2000). Assessors should also eschew the use of hypnosis to recover allegedly dissociated or repressed memories given that hypnosis does not enhance the overall accuracy of memories and is associated with a heightened risk for confabulation (Lynn, Knox, Fassler, Lilienfeld, & Loftus, 2004).

CASE EXAMPLE

CASE IDENTIFICATION AND PRESENTING COMPLAINTS

The patient, a 47-year old Caucasian female, first presented with dissociative symptoms to a health professional during a routine pelvic examination (see Colletti, Lynn, & Laurence, 2010 for a more complete description). During the exam, she exhibited dramatic changes in her demeanor. In quick succession, her emotions vacillated unpredictably, ranging from calm and composed, to scared and vulnerable, to angry and aggressive. The physician referred her for psychotherapy, insofar as her histrionic presentation was at sharp variance with what he observed during prior office visits.

HISTORY

When the patient initiated treatment with a psychotherapist, she insisted that her problems were the product of stress at work related to serious medical concerns (e.g., lupus, peripheral neuralgia, among others) that interfered with her job performance. Nevertheless, the therapist, a graduate student at a psychological clinic, noted that her mood and behavior fluctuated dramatically both within and between sessions, with episodes of anger and anxiety flaring up frequently and unpredictably within sessions. Over the next 2 years, the patient recounted a history of sexual assault 7 years prior to treatment, the death of a sibling, intense and sometimes unstable interpersonal relationships, and sexual abuse in childhood. Emotional outbursts during sessions escalated; seemingly innocuous statements by the therapist could trigger memories of highly aversive events. The patient began to experience more frequent crises in and out of sessions as well as emotional lability, often alternating between speaking in a childlike voice and an angry adult, only to later apologize and express deep regret. Her memory for what transpired when she appeared to be enacting different "identities" was spotty and at times devoid of meaningful content.

After 2 years of treatment, the graduate student transferred the case to his supervisor, who witnessed increased irritability, vitriolic anger, and flashback-like experiences

in session that were followed by amnesia, depersonalization, derealization, and problems in focusing attention. The patient reported feeling "spaced out" in session, and reported that she often was aware of "missing time" at home, and experienced difficulties recalling anything beyond the gist of the previous session. At the start of treatment with her second therapist, she met the criteria for borderline personality disorder, and DID was considered a rule-out diagnosis. She reported hearing "voices in my head" and experienced herself as "splitting off" into an angry "adult protector" or defender of others and childlike aspects of herself that required protection. One major diathesis for her dissociative symptoms appeared to be a history of fantasy versus reality-based coping originating in childhood. She became aware of this style of coping when her sister died when the patient was 5 years old, and she experienced guilt for not somehow preventing her death. She stated that she began, from that time forward, to think of herself as split into angry and protective "parts." As therapy progressed, she reported more frequent episodes of depersonalization and disturbing episodes of amnesia, as well as disorientation at times of high stress. She also reported more incidents of abuse during childhood, and her therapist felt her presentation now met criteria for DID.

At this time, Steven Jay Lynn, one of the authors of this chapter, was invited to serve as a consultant and co-therapist. The therapists conveyed the consistent message that although at times she felt as if she housed distinct personalities, she truly embodied only one personality. The therapists implemented a multifaceted treatment that included: (a) elements of affect management and problem-solving to contend with anger; (b) cognitive behavioral therapy (CBT techniques including activity scheduling for depressed mood, progressive muscle and hypnosis-based relaxation, and rational disputation of maladaptive thoughts); (c) mindfulness-based techniques for detaching from negative and self-deprecating cognitions and moods; and (d) affect containment methods derived from dialectical behavior therapy. After 4 years of treatment, the patient exhibited no signs of "personality split" and only occasional episodes of depersonalization, with improved functioning and mood stabilization.

Assessment

The patient met all the diagnostic criteria for DID, including her enacting distinct "identities" during sessions and reports of such alterations outside of sessions. She also reported amnesia associated with dissociative episodes, and was troubled by her failure to recall key interpersonal interactions that others remembered well. The patient was not assessed at the outset of treatment, although when SJL came onboard, she was evaluated with the DES and scored in the clinical range (i.e., 39) and met diagnostic criteria for DID based on the SCID-D (Steinberg, 1994).

ETIOLOGICAL CONSIDERATIONS

Behavioral Genetics

Limited research is available on the behavioral genetics of dissociative disorders. The evidence indicates that DID co-aggregates within biological families (APA, 1994), although data on intact family members are indeterminate with regard to genetic

versus shared environmental causation. Using twin registry data, Jang, Paris, Zweig-Frank, and Livesley (1998) reported that 48% of the variability in DES-T scores is attributable to genes, and that the other 52% of the variance can be attributed to nonshared environments. When the researchers considered nonpathological dissociation scores, excluding taxon items, genetic influences accounted for 55% of the variance, whereas nonshared environmental influences accounted for 45% of the variance. Similarly, a study of children and adolescents found a substantial genetic (59% genes, 41% nonshared environments) contribution to dissociation scores (Becker-Blease et al., 2004). In contrast, a study (Waller & Ross, 1997) based on 280 identical twins and 148 fraternal twins found no evidence for genetic influences. Approximately 45% of the variance on a measure of pathological dissociation (DES-T) was attributable to shared environmental influences, with the remaining variance due to nonshared environmental influences. Adoption studies would help to clarify the extent to which the familial clustering of dissociative disorders is due to genes, shared environment, or both.

BIOLOGY

Drugs, notably low doses of the anesthetic ketamine, often produce dream-like states and dissociative symptoms, suggesting that dissociative experiences need not necessarily arise in the aftermath of trauma. Krystal et al. (1994) found that ketamine produces alterations in the perception of time (i.e., slowing) and alterations in the vividness, form, and context of sensory experiences, all possibly attributable to diminished NMDA-related neurotransmission (Simeon, 2004). Interestingly, cannabinoids, including marijuana, which induce dissociative experiences, may similarly affect NMDA receptors (Simeon et al., 2003). The fact that hallucinogens (e.g., LSD), which frequently elicit depersonalization reactions in healthy participants, are agonists of serotonin 5-HT_{2A} and 5-HT_{2C} receptors implies that serotonin also may mediate dissociation (Simeon, 2004). Research that establishes links between drugs that produce dissociative symptoms in conjunction with changes in specific neurotransmitter systems hold the potential to shed light on the neurobiological basis of these dissociative symptoms (Giesbrecht et al., 2008). The pharmacological study of dissociation is important because it may shed light on the paradoxical phenomenon that detoxified opiate users exhibit higher dissociation scores than patients who are on a methadone maintenance regimen (Somer, Altus, & Ginzburg, 2010). One possible explanation for this pattern is the chemical dissociation hypothesis, that is, the notion that substance abuse patients achieve dissociative-like states through chemicals (e.g., alcohol, opiates), and in the absence of chemicals, they feel compelled to produce the dissociative symptoms themselves. This line of reasoning is consistent with pilot data suggesting that the opioid blocking drug naloxone is effective in reducing depersonalization experiences (Nuller, Morozova, Kushnir, & Hamper, 2001; but see Somer, Amos-Williams, & Stein, 2013).

Studies examining daytime EEG activity in highly dissociative individuals have generally found evidence that dissociative experiences are related to parameters signaling reduced attentional control (e.g., attenuated P300, Kirino, 2006; decreased theta activity; Krüger, Bartel, & Fletcher, in press). Sleep EEG recordings obtained in insomnia patients found suggestive evidence that dissociative psychopathology is

related to extended REM sleep (van der Kloet et al., 2013). It is tempting to relate lack of attentional control and extended REM to structural sleep disturbances, as suggested later in our discussion.

Simeon et al. (2000) used PET and MRI brain imaging to compare 8 participants with DDD with 24 healthy participants. The researchers found that depersonalization is associated with functional abnormalities in sequential hierarchical areas—secondary and cross modal—of the sensory cortex (visual, auditory, and somatosensory), as well as areas responsible for integrated body schemas. Specifically, DDD patients showed lower metabolic activity in right Brodmann areas 21 and 22 of the superior and middle temporal gyri, and higher metabolism in parietal Brodmann areas 7B and 39 and left occipital Brodmann area 19. The researchers contended that these findings are compatible with the phenomenological conceptualization of depersonalization as a dissociation of perceptions, as well as with the subjective symptoms of DDD.

In a fascinating study, Sang, Jáuregui-Renaud, Green, Bronstein, and Gresty (2006) showed that disorienting vestibular stimulation produced by caloric irrigation of the ear labyrinths engendered depersonalization in healthy participants and symptoms (e.g., feeling spaced out, body feels strange/not in control of self) similar to those experienced by patients with vestibular disease. The researchers suggested that depersonalization/derealization experiences may "occur because distorted vestibular signals mismatch with sensory input to create an incoherent frame of spatial reference which makes the patient feel that he or she is detached or separated from the world" (p. 760).

In a later study, the researchers (Jáuregui-Renaud, Sang, Gresty, Green, & Bronstein, 2008) found that patients with peripheral vestibular disease reported a higher prevalence of depersonalization/derealization symptoms and greater errors on a body rotation test of updating spatial orientation compared with healthy control participants. The investigators claimed that their findings support their theory that DDD symptoms sometimes reflect a mismatch between disordered vestibular input and other sensory signals of orientation. This claim was supported in a study in which patients with vestibular disease and patients with retinal disease reported more symptoms of depersonalization than patients with hearing loss and healthy participants (Jáuregui-Renaud, Ramos-Toledo, Aguilar-Bolaños, Montaño-Velazquez, & Pliego-Maldonado, 2008). Depersonalization and derealization experiences may well be the product of mismatches or lack of integration between multisensory inputs (e.g., vestibular, visual, proprioceptive) that produces dysfunctional neural representations that in turn generate an altered sense of self and reality (Aspell & Blanke, 2009).

Out-of-body experiences (OBEs), which are intimately related to depersonalization, are increasingly being studied in the laboratory (e.g., Ehrsson, 2007; Lenggenhager, Tadi, Metzinger, & Blanke, 2007) and are coming to be understood in terms of the scrambling of the senses (e.g., touch and vision) when people's usual experience of their physical body becomes disrupted. In addition, scientists are identifying the brain location of OBEs by stimulating the vestibular cortex, the superior temporal gyrus, and the place where the brain's right temporal and parietal lobes join (Blanke, Ortigue, Landis, & Seeck, 2002; Blanke & Thut, 2007; Cheyne & Girard, 2009; De Ridder, Van Laere, Dupont, Menovsky, & Van de Heyning, 2007; Persinger, 2001).

Ehrrson (2007) provided participants with goggles that permitted them to view a video display of themselves relayed by a camera placed behind them. This set-up created the illusion that their bodies, viewed from the rear, were standing in front of them. Ehrrson touched participants with a rod on the chest while he used cameras to make it appear that the visual image was being touched at the same time. Participants reported the eerie sensation that their video double was also being touched. In short, they reported that they could experience the touch in a location outside their physical bodies (see also Aspell, Lenggenhager, & Blanke, 2009; Lenggenhager et al., 2007). When visual sensory impressions combine with physical sensations, they can deceive people into believing that their physical selves are separate from their bodies (Cheyne & Girard, 2009; Terhune, 2009), suggesting a physiological genesis of at least some depersonalization experiences. Relatedly, disruptions in somatosensory signals may explain why some people experience OBEs during sleep paralysis (Nelson, Mattingly, Lee, & Schmitt, 2006) and during general anesthesia when they retain partial awareness (Bunning & Blanke, 2005). Nevertheless, researchers have little understanding of how stressors and other precipitants of depersonalization and derealization create and maintain the symptoms of dissociative disorders.

Researchers have devoted considerable attention to describing physiological differences among alters in DID and have reported interidentity differences in heart rates, voice pitch, eyeglass prescriptions, handedness, handwriting, allergies, or pain tolerance (see Lilienfeld & Lynn, in press). Nevertheless, it is unclear whether such differences validate the existence of alters, as many of these differences may merely reflect differences in mood, differences stemming from the unconscious role-playing of different identities, or both. Also, some authors have pointed out that one may obtain similar intra-individual differences when healthy actors are instructed to role-play alters (Boysen & VanBergen, in press; Merckelbach, Devilly & Rassin, 2002). Moreover, Allen and Movius (2000) suggested that some of these apparent differences might reflect Type I errors given the large number of psychophysiological variables analyzed in many of these studies.

Tsai, Condie, Wu, and Chang (1999) used MRI with a 47-year-old female with DID in an attempt to corroborate a history of childhood abuse. The authors drew upon previous investigations that had reported a reduction in hippocampal volume following combat trauma (e.g., Bremner, Randall, Scott, & Bronen, 1995) and early abuse (Bremner, Randall, Vermetten, & Staib, 1997; Stein, Koverola, Hanna, & Torchia, 1997) to hypothesize that DID patients—given their presumed history of early abuse—would similarly exhibit decreased hippocampal volume. As predicted, they found significant bilateral reductions in hippocampal volume in their patient with DID. Nevertheless, this finding must be interpreted cautiously for two major reasons (Lilienfeld & Lynn, in press). First, because it is based on only one patient, its generalizability to other individuals with DID is unclear. Second, decreased hippocampal volume is not specific to PTSD or to other conditions secondary to trauma, and has also been reported in schizophrenia (Nelson, Saykin, Flashman, & Riordan, 1988) and depression (Bremner et al., 2000). Consequently, decreased hippocampal volume may be a nonspecific marker of long-term stress (Sapolsky, 2000) that is present in many psychiatric conditions.

Learning, Modeling and Life Events

Some cases of (mis)diagnosed dissociative disorders are probably a product of malingering. Estimates suggest that malingering or other forms of feigning (e.g., the faking seen in factitious disorders) account for 2%–10% of diagnoses of inpatient dissociative disorders (Friedl & Draijer, 2000). There is widespread agreement that DID can be successfully malingered. For example, Kenneth Bianchi, one of the two Hillside Strangler murderers, is widely believed to have faked DID to escape criminal responsibility (Orne, Dinges, & Orne, 1984). In one survey, experienced neuropsychologists estimated the prevalence of feigned dissociative symptoms in cases involved in litigation to be about 10% (Mittenberg, Patton, Canyock, & Condit, 2002). Nevertheless, cases of malingered DID are believed to be quite rare outside of forensic settings, and the substantial majority of individuals with this condition do not appear to be intentionally fabricating their symptoms. Malingerers strive for advantages (e.g., financial, legal), but dissociative disorders are known to be associated with functional impairments that are so severe that they qualify as serious and often debilitating mental illnesses (Mueller-Pfeiffer et al., 2012).

THE POSTTRAUMATIC VERSUS THE SOCIOCOGNITIVE MODELS OF DISSOCIATION

There is little dispute that some individuals meet the diagnostic criteria for DID, display unpredictable and sometimes bizarre shifts in mood and behavior, and are convinced that they house compartmentalized "personalities" engendered by severe early physical abuse, sexual abuse, or both. Nevertheless, over the past 25 years, controversy has swirled around the question of whether the symptoms of DID are naturally occurring responses to early trauma (Dalenberg et al., 2012; Gleaves, 1996), as the posttraumatic model (PTM) of dissociation holds, or are largely socially constructed and culturally influenced, as the sociocognitive model (SCM)—called by some the fantasy model (Dalenberg et al., 2012)—of dissociation holds (Spanos, 1994). One commentator (Paris, 2012) has gone so far as to claim that DID is a fad that is now declining in interest in the psychiatric community, whereas others have vigorously challenged this assertion (Brand, Loewenstein, & Spiegel, 2013b; Martinez-Taboas, Dorahy, Sar, Middleton, & Krüger, 2013).

Proponents of the PTM (Gleaves, 1996; Gleaves et al., 2001; Ross, 1997) argue that DID is a posttraumatic condition that arises primarily from a history of severe physical and/or sexual abuse in childhood. Advocates of the PTM contend that such abuse is a crucial contributor to DID: The child compartmentalizes the abuse so that he or she feels as though it is happening to someone else (Ross, 1997). Moreover, alters or ego states supposedly arise as a means of coping with the intense emotional pain of the trauma [see Lilienfeld & Lynn (in press), for an explanation and critique]. PTM theories variously emphasize the effects of childhood abuse and early traumatic experiences on producing (a) patterns of disorganized interpersonal attachment (Liotti, 1999; 2009) that engender dissociation; (b) structural dissociation (i.e., the development of different "parts" of the personality to handle different functions in "defense" and everyday life; Steele, van der Hart, Nijenhuis, 2009); (c) disturbances

in the self-system that integrates "identity-mind-body-world-time" into a coherent whole; in this view, alters are conceptualized as "younger self-systems (ego-states) that are 'trapped' in a past trauma" (p. 283, Beere, 2009); (d) developmental deficits that degrade self-regulation and promote fragmentation of the self (Carlson, Yates, & Sroufe, 2009); and (e) a dissociative information processing style related to feelings of being betrayed by a trusted caregiver (Barlow & Freyd, 2009; Freyd, 1996).

These diverse theories are ostensibly supported by very high rates—sometimes exceeding 90%—of reported histories of severe child abuse among patients diagnosed with DID and other severe dissociative disorders (Dalenberg et al., 2012; Gleaves, 1996). Nevertheless, critics of the PTM (see Giesbrecht et al., 2008; Giesbrecht et al., 2010; Lilienfeld et al., 1999; Lynn et al., in press; Merckelbach & Muris, 2001; Spanos, 1994, 1996) have questioned the notion that DID is invariably linked to child abuse or maltreatment for the following five reasons:

1. Many studies that purport to confirm this association lack objective corroboration of child abuse (e.g., Coons, Bowman, & Milstein, 1988). For example, Sanders and Giolas (1991) found a correlation of $r = .44$ between the DES and scores on a child-abuse questionnaire. Yet when a psychiatrist (unaware of the dissociative status of participants) provided more objective ratings of trauma based on hospital records, the authors found a nonsignificant *negative* correlation between ratings of traumatic experiences and dissociation ($r = -.21$).
2. The overwhelming majority of studies investigating the link between self-reported trauma and dissociation are based on cross-sectional designs that do not permit causal inferences (Merckelbach & Muris, 2001) and that are subject to retrospective biases. Prospective studies that circumvent the pitfalls of retrospective reporting often fail to substantiate a consistent link between childhood abuse and dissociation in adulthood (Dutra, Bureau, Holmes, Lyubchik, & Lyons-Ruth, 2009; Noll, Trickett, & Putnam, 2003; Ogawa, Sroufe, Weinfield, Carlson, & Egeland, 1997; but see Bremner, 2010; Dalenberg et al., 2012).
3. Researchers rarely control for potentially comorbid psychopathological syndromes and symptoms known to be related to dissociative disorders (e.g., anxiety, eating, personality disorders, impulsivity, schizotypal traits; see Giesbrecht et al., 2008; Lynn et al., in press).
4. The reported high levels of child abuse among DID patients may be attributable to selection and referral biases common in psychiatric samples. For example, patients who are abused are more likely than other patients to enter treatment (Pope & Hudson, 1995).
5. Correlations between abuse and psychopathology tend to decrease substantially or disappear when participants' perception of family pathology is controlled statistically (Nash, Hulsey, Sexton, Harralson, & Lambert, 1993). Based on these five points of contention, Lilienfeld and Lynn (in press) noted that the available evidence provides little or no warrant for concluding that early abuse is a necessary causal antecedent of DID (see also Lynn et al., 2014).

In contrast to the PTM, proponents of the sociocognitive model (SCM; Spanos, 1994, 1996; see also Aldridge-Morris, 1989; Lilienfeld et al., 1999; Lynn et al., 2014; Lynn &

Pintar, 1997; McHugh, 1993; Merskey, 1992; Sarbin, 1995) contend that DID results from inadvertent therapist cueing (e.g., suggestive questioning regarding the existence of possible alters, hypnosis, sodium amytal), media influences (e.g., television and film portrayals of DID, such as "Sybil"), and broader sociocultural expectations regarding the presumed clinical features of DID.

Advocates of the SCM cite the following findings (Lilienfeld et al., 1999; Lilienfeld & Lynn, in press) as consistent with the SCM or as challenges to the PTM:

1. The number of patients with DID, along with the number of alters per DID individual, have increased dramatically over the past few decades (Elzinga, van Dyck, & Spinhoven, 1998; North et al., 1993), although the number of alters at the time of initial diagnosis appears to have remained constant (Ross, Norton, & Wozney et al., 1989).
2. The massive increase in reported cases of DID followed closely upon the release of the best-selling book *Sybil* (Schreiber, 1973) in the mid 1970s, which told the story of a young woman with 16 personalities who reported a history of severe child abuse at the hands of her mother. As noted earlier, in 1976, this book was turned into a widely viewed television film starring Sally Fields. Interestingly, however, a well-known psychiatrist who was involved closely with the Sybil case later contended that Sybil's presentation of DID was largely or entirely the product of therapeutic suggestion. Herbert Spiegel, who served as a backup therapist for Sybil, maintained that Sybil's primary therapist, Cornelia Wilbur, frequently encouraged her to develop and display different personalities in therapy. According to Rieber (2006), who possessed tapes of conversations between Sybil and Cornelia Wilbur, Spiegel referred to Sybil as a "brilliant hysteric," with multiple identities fabricated to please the all too credulous Wilbur. Spiegel further maintained that Wilbur and Flora Schreiber, who authored the best-selling book about Sybil, insisted that Sybil be described in the book as a "multiple" to make the book more appealing (Acocella, 1999). Rieber concluded "the three women—Wilbur, Schreiber, and Sybil—are responsible for shaping the modern myth of multiple personality disorder" (Rieber, 2006, p. 109). In short, increases in the diagnosis of DID and the number of alters per DID patient coincide with dramatically increased therapist and public awareness of the major features of DID (Fahy, 1988).
3. Mainstream treatment techniques for DID often reinforce patients' displays of multiplicity (e.g., asking questions like, "Is there another part of you with whom I have not spoken?"), reify alters as distinct personalities (e.g., therapists calling different alters by different names, mapping their "personality systems"), and encourage patients to establish contact and dialogue with presumed latent alters (Spanos, 1994, 1996). A case in point is the $N = 1$ within-subject study by Kohlenberg (1973), who showed that the behavioral displays of alter personalities can depend on reinforcement contingencies: The patient's alters soon "disappeared" after hospital staff stopped attending to them.
4. Many or most DID patients show few or no clear-cut signs of this condition (e.g., alters) prior to psychotherapy (Kluft, 1984).
5. The number of alters per DID individual tends to increase substantially over the course of DID-oriented psychotherapy (Piper, 1997) and there are indications

that this type of therapy might exacerbate symptoms (Fetkewicz, Sharma, & Merskey, 2000).
6. Psychotherapists who use hypnosis tend to have more DID patients in their caseloads than do psychotherapists who do not use hypnosis (Powell & Gee, 1999).
7. The majority of diagnoses of DID derive from a relatively small number of psychotherapists, many of whom are specialists in DID (Mai, 1995) and from a relatively small number of people in treatment (Boysen, 2011; Boysen & VanBergen, 2013; but see Brand, Loewenstein, & Spiegel, 2013b).
8. Laboratory studies suggest that nonclinical participants who are provided with appropriate cues and prompts can reproduce many of the overt features of DID (Spanos, Weekes, & Bertrand, 1985; Stafford & Lynn, 2002).
9. Until 20 years ago, diagnoses of DID were limited largely to North America, where the condition has received widespread media publicity (Spanos, 1996), although DID is now being diagnosed with considerable frequency in some countries (e.g., Holland) in which it has become more widely publicized since the 1990s. Manifestations of DID symptoms also vary across cultures. For example, in India, the transition period as the individual shifts between alter personalities is typically preceded by sleep, a presentation that reflects common media portrayals of DID in India (North et al., 1993). There are indications that both research interest in DID and media coverage of the condition are waning, and so it will be interesting to see whether this change heralds drops in prevalence rates (Pope, Barry, Bodkin & Hudson, 2006).
10. Laboratory research summarized below challenges the assertion that consciousness can be separated into multiple streams by amnesic barriers to form independently functioning alter personalities (Huntjens, Verschuere, & McNally, 2012; Kong, Allen, & Glisky, 2008; Lynn et al., 2004).

These 10 sources of evidence do not imply that DID can typically be created *in vacuo* by iatrogenic (therapist-induced) or sociocultural influences. SCM theorists acknowledge that iatrogenic and sociocultural influences typically operate on a backdrop of preexisting psychopathology, and exert their impact primarily on individuals who are seeking a causal explanation for their instability, identity problems, and impulsive and seemingly inexplicable behaviors. Indeed, the SCM is entirely consistent with findings, reviewed earlier, that many or most patients with DID meet criteria for borderline personality disorder, a condition marked by extremely labile behaviors.

Cognitive Mechanisms of Dissociation

Despite subjective reports of profound cognitive disturbances like amnesia, feelings of unreality, and identity alterations, researchers have found evidence for only relatively subtle and specific cognitive deficits in highly dissociative individuals. Such individuals usually fall within the normative range on tests of intellectual ability and standard neuropsychological tests (Giesbrecht et al. 2008; Schurle, Ray, Bruce, Arnett, & Carlson, 2007). Indeed, whereas most studies, with few exceptions (but see Prohl, Resch, Parzer, & Brunner, 2001), fail to report any link between dissociation and working memory capacity, some report that dissociative individuals exhibit *superior* verbal working memory capacity or performance (Giesbrecht et al., 2008).

When cognitive deficits in dissociative patients are identified, they tend to be quite specific. For example, Guralnik, Schmeidler, and Simeon (2000) found that DDD patients exhibited deficits in visual perception and visual-spatial reasoning for both two- and three- dimensional stimuli. Patients' visual and verbal short-term memory capacity was also compromised, for both abstract and meaningful information, especially under information overload conditions. DDD participants experienced difficulty with early stimulus-encoding tasks under conditions of heightened distraction, to which they responded with more omission errors. Accordingly, DDD appears to be characterized by vulnerability in early information processing at the level of perception and attention (for replications, see Guralnik, Giesbrecht, Knutelska, Sirroff, & Simeon, 2007; Quaedflieg et al., 2012).

Simeon and colleagues (Simeon, Hwu, & Knutelska, 2007) found evidence for a relationship between the dissociative symptoms of DDD patients, temporal disintegration (i.e., problems in memory regarding the chronology and dating of events), and total DES scores. They concluded that the dissociative dimension of absorption is a significant predictor of temporal disintegration.

The relative absence of a measurable general neuropsychological deficit in the dissociative disorders is noteworthy, as it differentiates them from most other severe psychiatric disorders, such as schizophrenia and bipolar disorder. These other conditions overlap with the dissociative disorders, but unlike them, are marked by a wide range of neuropsychological deficits (Heinrichs & Zakzanis, 1998). In addition, different dissociative disorders appear related to different cognitive deficiencies. DID is characterized mainly by performance fluctuations [e.g., increased scatter on the Wechsler Adult Intelligence Scale (Wechsler, 1981); Rossini, Schwartz, & Braun, 1996; reduced P300 amplitudes, but only during acute dissociative episodes in DID patients; Kirino, 2006], whereas DDD is associated with disruptions in early stages of information processing (Guralnik et al., 2000). Nevertheless, few investigations have controlled for general distress and psychopathology, or for scores on openness to experience, which is moderately associated with both dissociative tendencies (Kihlstrom, Glisky, & Angiulo, 1994) and with crystallized intelligence (DeYoung, Peterson, & Higgins, 2005). Interestingly, as we have noted earlier, dissociative individuals sometimes exhibit a performance advantage relative to nondissociative individuals (e.g., Chiu, Yeh, Huang, Wu, & Chiu, 2009).

Much of the literature on cognitive mechanisms of dissociation is more consistent with the SCM rather than the PTM. As already noted, proponents of the PTM typically argue that individuals who undergo horrific trauma in early life often dissociate or compartmentalize their personalities into discrete alters, segregated by amnesic barriers, as a means of coping with the intense emotional pain of the trauma. However, studies of amnesia among patients with DID have generally not reported findings commensurate with the existence of true amnesia among so-called alter personalities (Giesbrecht et al., 2010). For example, researchers have found little or no evidence for interidentity amnesia using objective measures (e.g., behavioral tasks or event related potentials) of memory (e.g., Allen & Movius, 2000; Huntjens et al., 2006; Huntjens et al., 2012; Huntjens, Peters, Woertman, van der Hart, & Postma, 2007; Kong et al., 2008).

If dissociative symptoms attenuate the impact of traumatic events, individuals with heightened levels of dissociation should exhibit slower or impaired processing of

threat-related information. Nevertheless, patients with DID and other "high dissociators" display *better* memory for to-be-forgotten sexual words in directed forgetting tasks (Elzinga, de Beurs, Sergeant, Van Dyck, & Phaf, 2000; see also Cloitre, Cancienne, Brodsky, Dulit, & Perry, 1996), a finding strikingly discrepant with the presumed defensive function of dissociation. Research on nonclinical samples (e.g., Candel, Merckelbach, & Kuijpers, 2003) showing that dissociation is not associated with inferior memory performance has been replicated in patients with DDD (Montagne et al., 2007). Studies of cognitive inhibition in high dissociative clinical (Dorahy, Irwin, & Middleton, 2002; Dorahy, Middleton, & Irwin, 2005; Dorahy, McCusker, Loewenstein, Colbert, & Mulholland, 2006) and nonclinical (Giesbrecht, Merckelbach, & Smeets, 2006) samples typically find a breakdown in such inhibition, which stands in sharp contrast with the widespread idea that amnesia (i.e., extreme inhibitory effect on memory) is a core feature of dissociation (Anderson et al., 2004). Research also finds mixed support at best for the contention that highly dissociative individuals are superior to low dissociators in dividing their attention. In two samples, Devilly et al. (2007) failed to replicate DePrince and Freyd's (2001) findings of superior forgetting of trauma-related words in high- versus low-dissociator college students in a divided attention task (see also Giesbrecht & Merckelbach, 2009). Giesbrecht et al., (2010) contended that the findings we have reviewed challenge the widespread assumption that dissociation is related to avoidant information processing and suggested that apparent gaps in memory in interidentity amnesia, or dissociative amnesia more generally, could reflect intentional failures to report (McNally, 2003; Pope et al., 2006).

Giesbrecht and colleagues (Giesbrecht et al., 2008; Giesbrecht et al., 2010) further argued that dissociation is marked by a propensity toward pseudomemories, possibly mediated by heightened levels of suggestibility, fantasy proneness, and cognitive failures. They noted that at least 10 studies from diverse laboratories have confirmed a link between dissociation and fantasy proneness (Giesbrecht, Merckelbach, Kater, & Sluis, 2007), and that heightened levels of fantasy proneness are associated with both the tendency to overreport autobiographical memories (Merckelbach, Muris, Horselenberg, & Stougie, 2000) and the false recall of aversive memory material (Giesbrecht, Geraerts, & Merckelbach, 2007).

These authors contended that the relation between dissociation and fantasy proneness may explain why individuals with high levels of dissociation are more prone than other individuals to develop false memories of emotional childhood events (e.g., a severe animal attack; Porter, Birt, Yuille, & Lehman, 2000), and further pointed to data revealing links between hypnotizability, dissociative symptoms (Frischholz, Lipman, Braun, & Sachs, 1992), and high scores on the Gudjonsson Suggestibility Scale (GSS: Gudjonnson, 1984; Merckelbach, Muris, Rassin, & Horselenberg, 2000; Wofradt & Meyer, 1998). Similarly, some researchers have shown that dissociation increases the risk of commission (e.g., confabulations/false positives, problems discriminating perception from vivid imagery, errors in response to misleading questions) rather than omission memory errors; the latter type of error is presumably associated with dissociative amnesia (Giesbrecht et al., 2008; Holmes et al., 2005). Nevertheless, findings pertinent to the relation between trait dissociation and false memory susceptibility are often mixed and not invariably strong in magnitude (see Dalenberg et al., 2012; Lynn et al., 2014).

Taken together with research demonstrating a consistent link between dissociation and cognitive failures (Merckelbach, Horselenberg, & Schmidt, 2002; Merckelbach, Muris, & Rassin, 1999; Wright & Osborne, 2005), the findings summarized above point to an association between heightened risk of confabulation and possibly pseudomemories that raise questions regarding the accuracy of retrospective reports of traumatic experiences. In addition, these findings limit the inferences that we can draw from studies that rely exclusively on self-reports to establish a connection between trauma and dissociation (Merckelbach & Jelicic, 2004; Merckelbach et al., 2000).

Still, these findings do not exclude some role for trauma in the genesis of dissociation and dissociative disorders. Suggestibility, cognitive failures, and fantasy proneness might contribute to an overestimation of a genuine, although perhaps weak or modest, link between dissociation and trauma. Alternatively, early trauma might predispose individuals to develop high levels of fantasy proneness (Lynn, Rhue, & Green, 1988), absorption (Tellegen & Atkinson, 1974), or related traits. In turn, such traits may render individuals susceptible to the iatrogenic and cultural influences posited by the SCM, thereby increasing the likelihood that they will develop DID following exposure to these influences. This and even more sophisticated etiological models of DID have yet to be subjected to direct empirical tests. In the next section, we examine a novel theory that provides a possible basis of rapprochement between the PTM and the SCM.

Sleep, Memory, and Dissociation

A theory originally formulated by Watson (2001) linking sleep, memory failure, and dissociation may provide a conceptual bridge between the PTM and the SCM. In a review of 19 studies, van der Kloet, Merckelbach, Giesbrecht, and Lynn (2012) concluded that the extant research provides strong support for a link between dissociative experiences and a labile sleep-wake cycle that is evident across a range of phenomena, including waking dreams, nightmares, and hypnogogic (occurring while falling asleep) and hypnopompic (occurring after falling sleep) hallucinations. Studies that offered evidence for a link between dissociative experiences and sleep disturbances relied on clinical and nonclinical samples, and, with only one exception, yielded correlations in the range of 0.30–0.55, suggesting that unusual sleep experiences and dissociation are discriminable yet related constructs. Moreover, researchers (Giesbrecht, Smeets, Leppink, Jelicic, & Merckelbach, 2007) have shown that sleep loss induced in the laboratory intensifies dissociative symptoms, suggesting a possible causal link between sleep experiences and dissociation.

These findings suggest an intriguing interpretation of the link between dissociative symptoms and deviant sleep phenomena (see also Watson, 2001). Individuals with a labile sleep-wake cycle—perhaps associated with a genetic propensity or perhaps a byproduct of intrusions of trauma related memories—experience intrusions of sleep phenomena (e.g., dreamlike experiences) into waking consciousness, which in turn foster fantasy proneness, depersonalization, and derealization. These disruptions of the sleep-wake cycle, in turn, degrade memory (Hairston & Knight, 2004) and attentional control (Williamson, Feyer, Mattick, Friswell, & Finlay-Brown, 2001), thereby accounting for, or contributing to, the attention deficits and cognitive

failures evidenced by highly dissociative individuals (Giesbrecht, Merckelbach, Geraerts, & Smeets, 2004) and dissociative patients (Dorahy et al., 2006; Guralnik et al., 2007).

Accordingly, the sleep-dissociation perspective may explain both (a) how highly aversive events disrupt the sleep-cycle and increase vulnerability to dissociative symptoms, and (b) why dissociation, trauma, fantasy proneness, and cognitive failures overlap. Thus, the sleep-dissociation perspective is commensurate with the possibility that trauma mediated by sleep disturbances plays a pivotal role in the genesis of dissociation, and suggests that previously competing theoretical perspectives may be amenable to integration. The SCM holds that patients become convinced they possess separate indwelling identities as a byproduct of suggestive media, sociocultural, and psychotherapeutic influences. These patients' sensitivity to suggestive influences may arise from their propensity to fantasize, memory errors, increased salience of negative memories, and difficulties in distinguishing fantasy and reality brought about by disruptions in the sleep cycle.

Signs of Theoretical Convergence

Recently, signs are emerging of a modicum of convergence or rapprochement between competing theoretical perspectives. On the one hand, adherents of the PTM (Dalenberg et al., 2012) acknowledge that (a) "DID is a disorder of self-understanding" (p. 568) and that "those with DID have the inaccurate idea that they are more than one person" (p. 568); (b) the potential effects of trauma on dissociation are difficult to completely parcel out from harms caused by a pathogenic family environment; (c) biological vulnerabilities, psychiatric history, social support, and prenatal factors probably contribute to the genesis of dissociation; and (d) fantasy proneness may lead to inaccurate trauma reports. On the other hand, proponents of the SCM (Lynn et al., 2014) currently acknowledge that (a) trauma may play a nonspecific role in dissociation (e.g., by increasing stress levels); (b) laboratory support for the link between false memories and dissociation is mixed and not consistently impressive in magnitude; (c) traumatic events may produce memory fragmentation due to failures to encode significant events; and (d) therapeutic approaches to treat dissociation may be helpful, although the mechanisms by which improvement occurs have yet to be delineated and isolated from nonspecific effects of psychotherapy in the context of randomized clinical trials. The fact that divergent perspectives concur that multiple causal antecedents, and not merely early trauma, need to be considered to provide a comprehensive account of dissociation and dissociative disorders is a welcome development.

Treatment

Depersonalization and Derealization The available research evidence provides few guidelines for the treatment of dissociative disorders. Pharmacological treatments have proven to be of little help in improving symptoms of DDD or other dissociative disorders (Somer, Amos-Williams, & Stein, 2013). For example, only a small proportion of people with DDD exhibit a clinically meaningful or even partial response to selective serotonin reuptake inhibitors or benzodiazepines. Although stimulant

medications may improve concentration in individuals with DDD, they have little effect on the core symptoms of depersonalization (Simeon, et al., 1997, 2003). Moreover, the symptoms of depersonalization are no more responsive to fluoxetine (Simeon, Guralnik, Schmeidler, & Knutelska, 2004) or lamotrigine (Sierra, Phillips, Krystal, & David, 2003) than they are to a placebo. According to Simeon (2009b), the well-documented lack of response to anxiolytics or mood stabilizers among DDD patients suggests that this condition cannot be reduced to a mood or anxiety spectrum disorder, "despite being often triggered by, or co-occurring with, the latter" (p. 439). Nevertheless, the fact that treatment response differs across disorders does not necessarily preclude commonalities in etiology.

The literature on psychotherapy with patients with DDD is similarly scant. An open study conducted by Hunter, Baker, Phillips, Sierra, and David (2005) examined the effects of cognitive-behavioral therapy (CBT) in DDD. The investigators taught patients to interpret their symptoms in a nonthreatening way. Although there were dramatic improvements in the patient sample and follow-up results were on the whole promising, the results must be interpreted with caution given the absence of a randomized control group. More rigorous trials are needed to confirm the merits of CBT and other psychotherapeutic approaches in patients with DDD.

Dissociative Identity Disorder Individuals with DID typically are in treatment for an average of 6 to 7 years before being diagnosed with this condition (Gleaves, 1996). Advocates of the PTM see this finding as evidence that individuals with DID are underdiagnosed, whereas advocates of the SCM see it as evidence that patients who are later diagnosed with DID typically enter treatment with few or no symptoms of the disorder. The treatment outcome literature for DID is sparse. According to Brand, Classen, McNary, and Zaveri (2009), only eight studies have examined treatment outcomes for DID and other dissociative disorders. More recently, Brand's research team (Brand, Classen, Lanius, et al., 2009) reported a naturalistic study of DID and DD-NOS treatment by community clinicians. Nevertheless, there are no randomized controlled trials on DID. Furthermore, studies do not permit an evaluation of the extent to which symptom reduction in dissociative patients is due to regression to the mean, the passage of time, placebo effects, or other artifacts. Other methodological problems include variability in treatments offered to patients (e.g., Choe & Kluft, 1995), lack of controls for nonspecific effects (e.g., Ellason & Ross, 1997), dropout rates as high as 68% (Gantt & Tinnin, 2007), and the failure to document clinically meaningful changes following treatment. As a consequence, one cannot draw confident conclusions regarding treatment efficacy from the extant literature.

Importantly, some literature suggests that patients treated with commonly used DID interventions that involve identifying alters, addressing "parts," and recovering memories deteriorate significantly over the course of treatment. In one study, the majority of patients developed "florid posttraumatic stress disorder during treatment" (Dell & Eisenhower, 1990, p. 361). Moreover, after treatment commences, patients report increased suicide attempts (Fetkewicz et al., 2000), hallucinations, severe dysphoria, and chronic crises (Piper & Merskey, 2004). Nevertheless, Brand and Loewenstein (in press) contended that their analysis of treatment outcomes indicates that DID treatment, including interacting with "dissociated self states," improves

clinical outcomes and that depriving DID patients of treatment may cause "iatrogenic harm." Studies that compare negative sequelae across DID and conventional therapies are a priority.

Assuming that future studies establish that certain sleep deviations serve as causal antecedents of dissociative symptoms, it will be imperative to study the effects of treatment interventions focused on sleep normalization in dissociative patients (Hamner, Broderick, & Labbate, 2001; Merckelbach & Giesbrecht, 2006). Previous studies that have examined the effectiveness of sleep medication in PTSD (Van Liempt, Vermetten, Geuze, & Westenberg, 2006), DID (Loewenstein, Hornstein, & Farber, 1988) and dissociative symptoms in a mixed inpatient group (van der Kloet, Giesbrecht, Lynn, Merckelbach, & de Zutter, 2012) have yielded promising results.

CONCLUSION

Dissociative disorders and conditions, especially DID and dissociative fugue, are among the most controversial in all of descriptive psychopathology, and for good reason. Although dissociation is unquestionably a genuine subjective experience, serious questions remain concerning the assessment, etiology, and treatment of most dissociative disorders. The difficulties of diagnosing DID have led some workers in the field to question whether the disorder can be reliably diagnosed. Piper and Merskey (2004), for example, went so far as to write that patients ". . . with manifestations that are visible to only some clinicians and on only some occasions; with symptoms that cannot be distinguished from other psychiatric disorders or from malingering; with unacceptably vague diagnostic criteria; and with patients who initially deny their symptoms, show no signs of the condition's essential feature, and know nothing of either their traumatic histories or the presence of alters—simply cannot be reliably diagnosed" (p. 681; but see Gleaves et al., 2001, for a competing view). Although this might prove to be an extreme or unwarranted conclusion with respect to *DSM-5*, studies ascertaining the reliability and validity of dissociative disorder diagnoses are obviously a high priority.

Etiological issues are a particular sticking point, and appear no closer to resolution with the publication of *DSM-5*. Although some authors (e.g., Dalenberg et al., 2012; Gleaves, 1996) maintain that DID and perhaps other dissociative disorders stem primarily from early child abuse and maltreatment, others (e.g., Spanos, 1994) maintain that these conditions are largely socially and culturally influenced products that are aided and abetted by therapist prompting and cueing of symptoms—a view that is supported by multiple sources of circumstantial evidence (Lilienfeld et al., 1999). It remains to be seen whether new and promising models, such as those linking sleep deprivation to dissociative symptoms (van der Kloet et al., 2012), may provide common ground between these competing theories of the genesis of dissociative disorders. In the meantime, clinicians who work with dissociative patients should bear in mind the powerful historical lesson imparted by the literature on DID: in their well-meaning efforts to unearth psychopathology, assessors and therapists may inadvertently end up creating it (Lilienfeld et al., 1999).

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CHAPTER 12

Somatic Symptom and Related Disorders

GORDON J. G. ASMUNDSON, MICHEL A. THIBODEAU, and DANIEL L. PELUSO

DESCRIPTION OF THE DISORDERS

The somatic symptom and related disorders, as described in the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (*DSM-5*, American Psychiatric Association [APA], 2013), include somatic symptom disorder, illness anxiety disorder, conversion disorder (functional neurological symptom disorder), psychological factors affecting other medical conditions, factitious disorder, other specified somatic symptom and related disorder, and unspecified somatic symptom and related disorder. The somatic symptom and related disorders reconceptualize and replace the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition, text revision (*DSM-IV-TR*; APA, 2000) somatoform disorders. Changes were made in an effort to eliminate overlap and clarify boundaries between diagnosable disorders, and to recognize that people meeting diagnostic criteria for one of these disorders may or may not have an identifiable medical condition.

The following changes were made in the *DSM-5*: (a) conversion disorder (functional neurological symptom disorder) remains but now emphasizes the importance of the neurological exam; (b) body dysmorphic disorder was reconceptualized as a *DSM-5* obsessive-compulsive and related disorder (thereby moving it to a different category); (c) psychological factors affecting other medical conditions and factitious disorder, each included in different sections of the *DSM-IV*, have been added to this category; and (d) each of somatization disorder, undifferentiated somatization disorder, pain disorder, and hypochondriasis have been removed as diagnosable conditions and are subsumed under one of somatic symptom disorder, illness anxiety disorder, or psychological factors affecting other medical conditions. Importantly, unlike somatization disorder and hypochondriasis as defined in the *DSM-IV-TR*, the key disorder included in this new category (i.e., somatic symptom disorder) no longer requires medically unexplained symptoms as a core feature; instead, emphasis is placed on the impact of symptoms on cognition, emotion, and behavior. Although not without controversy (e.g., Frances, 2013; Frances & Chapman, 2013; Sirri & Fava, 2013; Starcevic, 2013), the Somatic Symptom Workgroup has suggested that aforementioned changes were made

in an effort to increase utility for the primary care and other medical (nonpsychiatric) clinicians to whom patients with somatic sensations or changes often present, to reduce stigma, to reduce promotion of mind-body dualism, to improve therapeutic alliance, and to facilitate correct diagnosis and good treatment outcomes (e.g., Dimsdale et al., 2013).

The common feature of the somatic symptom and related disorders is prominent somatic sensations (e.g., dyspnea, pain) or changes (e.g., subcutaneous lumps, rash)—called "symptoms" in *DSM-5* terminology—that are associated with significant emotional distress and functional impairment and often interpreted by the person as being symptomatic of some disease process or physical anomaly. Bodily sensations and changes are a common experience of day-to-day living for most people, and they typically remit without medical attention; however, about 25% of the population seeks medical attention when these sensations and changes persist (Kroenke, 2003). Up to 30% of those seeking medical attention will exhibit clinically significant distress about having an unidentified disease when there is no medical explanation for presenting "symptoms" (Fink, Sørensen, Engberg, Holm, & Munk-Jørgensen, 1999); yet, many remain distressed despite identifiable medical explanation (APA, 2013; Taylor & Asmundson, 2004). This distress is associated with substantial impairment of personal, social, and professional functioning as well as considerable costs to health care (Hessel, Geyer, Hinz, & Brahier, 2005), even after controlling for medical and psychiatric comorbidity (Barsky, Orav, & Bates, 2005).

Despite prevalence and cost of distressing somatic sensations and changes, as well as a substantive increase in empirical attention during the past decade, their presentation remains not well understood. Likewise, although there are some data on the validity, reliability, and clinical utility of somatic symptom disorder (Dimsdale et al., 2013), there have been few studies on the diagnostic category as a whole. In the sections that follow, we provide an overview of the general clinical profile, diagnostic considerations, and epidemiology of the *DSM-5* somatic symptom and related disorders. We then turn attention to issues of assessment, etiological considerations, and course and prognosis. In each of these latter sections, we touch on issues germane to the collective category as well as its specific disorders. In the case study, we focus more specifically on an illustration of uncomplicated somatic symptom disorder. As there is currently little data on epidemiology, etiology, course, prognosis, assessment, or treatment of the disorders included in this new *DSM-5* category, much of the data presented below is borrowed from pre-*DSM-5* knowledge of related conditions and disorders.

CLINICAL PICTURE

The clinical profile for each somatic symptom and related disorder is unique, although each disorder is predicated on the prominence of somatic sensations or changes associated with distress and impairment. A brief overview of the clinical profile of each somatic symptom disorder is provided, along with reference to *DSM-5* diagnostic criteria.

Somatic Symptom Disorder

Somatic symptom disorder is the cornerstone diagnosis of the somatic symptom and related disorders category. The main feature of somatic symptom disorder is the

presence of one or more somatic symptoms or features that cause distress and impairment in daily living (Criterion A). The concern ranges from highly specific (e.g., "This pain in my gut is so bad. I must have stomach cancer") to vague and diffuse (e.g., "My whole body is aching. What could it be? Maybe it's ALS."). Individuals with somatic symptom disorder exhibit excessive thoughts, feelings, or behaviors related to their somatic symptoms (Criterion B). An individual meets Criterion B if he or she: (a) exhibits disproportionate thoughts about the seriousness of their symptoms, (b) experiences persistently high levels of anxiety regarding their symptoms or about their health, or (c) devotes an excessive amount of time to their health (e.g., seeking reassurance from health professionals, doing research about their somatic sensations or changes, perusing body parts to find potential lumps). Excessive somatic concerns must persist for at least 6 months (Criterion C), although somatic symptoms do not need to be present for this entire period. Individuals with somatic symptom disorder may often resist the idea that they are suffering from a mental health disorder and may come to rely on reassurance seeking and checking behaviors (e.g., palpating subcutaneous lumps, searching for information about disease in medical textbooks and on the Internet) to placate concerns about having a serious disease. Although these behaviors can be effective in providing short-term relief, they perpetuate the condition in the long term (Taylor & Asmundson, 2004).

Somatic symptom disorder can be associated with a few diagnostic specifiers. An individual whose somatic complaints revolve largely around pain can receive a *with predominant pain* specifier. This specifier replaces the *pain disorder* diagnosis from *DSM-IV*. A *persistent* specifier can apply in cases wherein severe symptoms and impairment last for longer than 6 months. Finally, severity can be specified as *mild*, *moderate*, or *severe* when an individual meets one, two, or three of the Criterion B symptoms, respectively. For example, a *moderate severity* specifier could be assigned to an individual who reports debilitating anxiety due to bodily symptoms and who checks their body for hours a day to ensure no new blemishes have appeared.

Illness Anxiety Disorder

Illness anxiety disorder involves preoccupation with having or acquiring a serious illness (Criterion A). For example, an individual may fear contracting HIV or having recently contracted the virus. Illness anxiety disorder differs from somatic symptom disorder in that somatic symptoms are not present or are only minor (Criterion B). If minor somatic symptoms are present (e.g., light pain, minor bruising), the individual's distress is clearly out of proportion to the actual threat and focuses more on the meaning of the symptoms (e.g., consequences of having diabetes) rather than the somatic symptoms themselves. Individuals with illness anxiety disorder experience a great deal of distress rooted in their disease-related preoccupations and are easily alarmed about health-related matters (Criterion C). To illustrate, an individual with illness anxiety disorder may be excessively distressed when learning that a colleague or stranger has contracted cancer. Individuals with illness anxiety disorder participate in excessive behaviors aimed at reducing their anxiety (Criterion D), often bodily checking (e.g., looking for lesions that could be signs of an infection), reassurance seeking (e.g., repeatedly seeking medical testing), health-related research (e.g., reading about HIV on the Internet), and avoidance (e.g., avoiding hospitals as these could house harmful germs). These behaviors may placate concerns in the short term but,

ultimately, serve to reinforce disease-related preoccupation (Taylor & Asmundson, 2004). A diagnosis of illness anxiety disorder is contingent on illness anxiety lasting at least 6 months (Criterion E), although the focus of the anxiety may change during this time (e.g., from HIV to syphilis). Finally, the symptoms of illness anxiety disorder must not be better explained by another diagnosis (Criterion F), such as somatic symptom disorder, panic disorder, or obsessive-compulsive disorder. Illness anxiety disorder can be associated with one of two contrasting specifiers. The *care-seeking type* specifier can be applied when individuals frequently seek medical care. The *care-avoidant type* specifier can be applied when individuals rarely use medical care.

Conversion Disorder (Functional Neurological Symptom Disorder)

Conversion disorder involves the manifestation of altered voluntary motor or sensory functioning (Criterion A). Motor symptoms can include paralysis, paresthesia, tremors, convulsions, and abnormal movements or posture. Sensory symptoms can include blindness, altered or reduced hearing, unusual or inconsistent skin sensations, and altered speech patterns. The hallmark of conversion disorder is a lack of correspondence between signs and symptoms and medical understanding of the possible neurological condition (Criterion B). For example, an individual may display symptoms very consistent with epileptic seizures, but lack electrical activity in the brain consistent with epilepsy. Such an inconsistency is needed for a diagnosis. A lack of neurological evidence for reported or observed symptoms is not sufficient (e.g., trembling without any apparent brain damage). Symptoms of conversion disorder must not be better explained by another mental health or medical disorder (Criterion C) and the symptoms must cause clinically significant distress or impairment or warrant medical evaluation (Criterion D).

People with conversion disorder are often unaware of psychological factors associated with their condition, and many report an inability to control their symptoms. Although not a criterion for diagnosis of conversion disorder, lack of worry or concern about symptoms (i.e., *la belle indifference*) is mentioned in the *DSM-5* list of associated features. The available literature, however, fails to support the use of *la belle indifference* as a means of discriminating between conversion disorder and symptoms of organic pathology (Stone, Smyth, Carson, Warlow, & Sharpe, 2006).

Observed signs and symptoms of conversion disorder often appear to represent patient beliefs about how neurological deficits should present, rather than how neurological diseases actually function (Hurwitz, 2004). Onset typically follows a period of distress, such as that stemming from trauma (McFarlane, Atchison, Rafalowicz, & Papay, 1994; Roelofs, Keijsers, Hoogduin, Naring, & Moene, 2002; Van der Kolk et al., 1996) or physical injury (Stone et al., 2009). Diagnosis of conversion disorder can be associated with the specifiers *with psychological stressor* or *without psychological stressor*. Moreover, a specifier of *acute episode* or *persistent* can be applied when an individual's symptoms present for less or more than six months, respectively.

Psychological Factors Affecting Other Medical Conditions

A diagnosis of psychological factors affecting other medical conditions can apply in individuals who suffer from a medical condition (Criterion A) that is adversely

affected by psychological or behavioral factors (Criterion B). The effects on the medical condition can increase the odds of suffering, disability, or death. Psychological or behavioral factors can be deemed as detrimental if meeting one of the following conditions: (a) the psychological or behavioral factors preceded the development or worsening of the medical condition, or delayed recovery from the condition (e.g., repeatedly exacerbating an injury following discharge from hospital), (b) the factors interfere with treatment, (c) the factors are well established health-risks, or (d) the factors influence medical pathology, thereby exacerbating symptoms or requiring medical attention. Psychological or behavioral factors can include distress, maladaptive interpersonal patterns, and poor treatment adherence. The psychological or behavioral factors must not be subsumed within another mental disorder (Criterion C); thus, worsening of a medical condition due to panic disorder or due to substance abuse would not meet criteria for psychological factors affecting other medical conditions. Clinicians can apply specifiers reflecting *mild* (increases medical risk), *moderate* (aggravates medical condition), *severe* (results in hospitalization or emergency attention), or *extreme* (life threatening risk) influence of psychological factors on a medical condition.

Factitious Disorder

Factitious disorder imposed on self is a condition wherein an individual acts as if they have physical or psychological signs of an illness by producing, feigning, or exaggerating symptoms (Criterion A). The individual must present himself or herself as ill or impaired (Criterion B) and a diagnosis is contingent on identifying that the individual is actively misrepresenting their condition. Moreover, the deceptive behavior must occur without any obvious external rewards (Criterion C), such as monetary compensation or reduced responsibilities. A diagnosis of factitious disorder can be assigned to individuals who have a medical condition; but, in this case, the deceptive behavior is intended to make the person appear even more ill. The deceptive behavior cannot be better explained by another disorder, such as schizophrenia or delusional disorder (Criterion D). Individuals with factitious disorder may produce or exaggerate symptoms by consuming drugs (e.g., insulin, hallucinogens), injecting themselves with noxious substances (e.g., bacteria), contaminating blood and urine samples, or reporting symptoms that have never occurred (e.g., seizures). A specifier of *recurrent episodes* applies in cases wherein individuals have exhibited deceptive behavior more than once.

A separate diagnosis, referred to as factitious disorder imposed on another, can also be assigned. The criteria for this diagnosis are the same as factitious disorder, but a person other than the victim conducts the deceptive behavior. For example, a father may tamper with the urine sample of his child to misrepresent the child's health status. In this case, the parent would be assigned the diagnosis, not the child.

Other Specified Somatic Symptom and Related Disorder and Unspecified Somatic Symptom and Related Disorder

Other specified somatic symptom and related disorder applies to individuals who present with distressing or impairing symptoms that are similar to one of the somatic

symptom and related disorders but that do not fully satisfy the criteria for a diagnosis. The *DSM-5* presents four examples of specific disorders that can be used with the *other specified* disorder diagnosis. These include brief somatic symptom disorder, which can be assigned when an individual meets diagnostic criteria for somatic symptom disorder, but for less than 6 months; brief illness anxiety disorder, which can be assigned when symptoms of illness anxiety disorder last for less than 6 months; illness anxiety disorder without excessive health-related behaviors, which can be assigned when an individual meets all criteria for illness anxiety disorder except Criterion D; and, pseudocyesis, which can be assigned in individuals with a false belief of being pregnant that is associated with objective and reported signs of pregnancy (e.g., morning sickness, breast tenderness). A diagnosis of unspecified somatic symptom and related disorder can be applied when an individual presents with distressing or impairing symptoms that are similar to a somatic symptom and related disorder, but that do not meet the diagnostic criteria for any of the somatic symptom and related disorders.

DIAGNOSTIC CONSIDERATIONS (INCLUDING DUAL DIAGNOSIS)

To qualify for a somatoform disorder diagnosis under the *DSM-IV-TR*, somatic signs and symptoms were required to be medically unexplained; that is, somatic signs and symptoms could not be explained by organic pathology or physical deficit (APA, 2000). Sykes (2006) has argued that default attribution of medically unexplained somatic symptoms to psychopathology is untenable and has contributed to unjustified diagnoses of conditions characterized by somatic complaints as mental rather than physical disorders. In addition to supporting the perspective offered by Sykes (2006), and suggesting that diagnoses based on the absence of medically explained symptoms promoted stigma, the Somatic Symptom Workgroup pointed out that the reliability of establishing that somatic symptoms are not due to a general medical condition is low (e.g., Dimsdale et al., 2013). In the new classification system, somatic symptom disorder is now defined on the basis of positive symptoms (i.e., distressing somatic symptoms that present along with "observable" cognitions, emotions, and behaviors in response to the somatic symptoms); consequently, it is possible for people presenting with and without a diagnosable general medical condition to satisfy diagnostic criteria for the disorder. Medically unexplained symptoms only remain relevant to conversion disorder and other specified somatic symptom and related disorder (i.e., pseudocyesis) where it is possible to demonstrate inconsistency between presenting symptoms and medical pathology.

In arriving at a diagnosis of one of the somatic symptom and related disorders it is important to consider that there are multiple sources of distressing somatic sensation and changes. First, a number of mental health disorders are characterized by somatic symptoms (e.g., depression, panic disorder, posttraumatic stress disorder) and may either account for or accompany the somatic symptoms. In the former case a somatic symptom and related disorder diagnosis would not be warranted, whereas in the latter case a dual diagnosis would be warranted. Likewise, given that distressing somatic symptoms often occur in response to a general medical condition such as cancer or multiple sclerosis, considerable care is warranted in establishing whether the response is psychopathological in nature. Some critics of the *DSM-5* fear that

diagnostic thresholds have been loosened to the point where clinicians will be challenged in distinguishing normal from psychopathological responses in those with distressing somatic symptoms stemming from a medical condition, resulting in overdiagnosis of somatic symptom disorders (Frances, 2013). Finally, it is important to recognize that many benign physical factors can give rise to somatic signs and symptoms. Consider, for example, physical deconditioning. People concerned by somatic sensations often avoid physical exertion, including aerobic and anaerobic exercise, for fear that it will have harmful consequences. As a result, they become physically deconditioned. Physical deconditioning is associated with postural hypotension, muscle atrophy, and exertion-related breathlessness and fatigue, all of which can promote further inactivity and reinforce beliefs that one is ill (Taylor & Asmundson, 2004).

Further research is required to determine whether the modifications made in the *DSM-5* will facilitate accuracy of diagnoses relative to that attainable with the *DSM-IV-TR* somatoform disorders. The importance of diagnosis cannot be overstated, as any diagnosis carries significant implications for individuals receiving the diagnosis and their related experiences (e.g., stigmatization, interpretation of symptoms, nature of treatment, response to treatment). As Kirmayer and Looper (2007) note, diagnosis is a form of intervention and, as such, is a crucial element in shaping treatment and outcome.

EPIDEMIOLOGY

Somatic symptom and related disorders are often associated with true or perceived organic pathology; consequently, this class of disorders is a challenge to diagnose and to study from an epidemiological standpoint due to difficulties in thoroughly assessing the mind and body. Given the substantial changes in diagnostic criteria between the *DSM-III and DSM-5*, providing precise epidemiological prevalence rates for somatic symptom and related disorders is extremely challenging. Indeed, the somatoform disorders were not included in the large-scale national comorbidity surveys based on *DSM-III-R* (Kessler, 1994) and *DSM-IV-TR* criteria (Kessler, Chiu, Demler, Merikangas, & Walters, 2005), nor were they examined in the World Health Organization World Mental Health Surveys initiative (Kessler & Üstün, 2008), which further limits inferences regarding the somatic symptom and related disorders. Moreover, epidemiological researchers have often paired somatoform disorders with other disorders (e.g., anxiety disorders; Bland, Orn, & Newman, 1988) or have excluded specific disorders from analyses due to low or high base rates or differences in classification methodologies (Leiknes, Finset, Moum, & Sandanger, 2008). As such, the prevalence of somatic symptom and related disorders as a class of disorders remains almost entirely unstudied and our knowledge at this time can only be extrapolated from earlier research on the somatoform disorders.

The somatic symptom and related disorders are substantially different from the somatoform disorders described in *DSM-IV-TR*; however, some of the broader epidemiological findings likely still hold true. For example, presentation of somatic concerns that do not meet diagnostic criteria for a somatoform disorder or medical condition account for approximately half of all physician visits (Nimnuan, Hotopf, & Wessely, 2001), suggesting that subsyndromal somatic symptoms are highly

prevalent and costly (Barsky et al., 2005; Kirmayer & Robbins, 1991). Somatic symptom and related disorders are likely more common in women (Wittchen & Jacobi, 2005), with perhaps the exception of somatic symptom disorder, which appears to have similar prevalence in both genders based on the rates of hypochondriasis (Asmundson, Taylor, Sevgur, & Cox, 2001; Bleichhardt & Hiller, 2007). People with a somatic symptom and related disorder are also very likely to frequently experience co-occurring mood disorders (Leiknes et al., 2008), anxiety disorders (Lowe et al., 2008), personality disorders (Bornstein & Gold, 2008; Sakai, Nestoriuc, Nolido, & Barsky, 2010), as well as other somatic symptom and related disorders (Leiknes et al., 2008).

Somatic symptom disorder encapsulates approximately 75% of individuals who previously met diagnostic criteria for hypochondriasis (APA, 2013), and likely represents the most prevalent of the somatic symptom and related disorders. Somatic symptom disorder has a prevalence of approximately 5% to 7% in the general population (APA, 2013), which is consistent with the 12-month prevalence rate of 4.5% for hypochondriasis (Faravelli et al., 1997). Research on hypochondriasis suggests that somatic symptom disorder is likely more common in primary care settings. Reported prevalence rates of hypochondriasis in primary care settings have varied considerably based on methodology. Studies using diagnostic interviews have reported a point prevalence of 3% (Escobar et al., 1998) and a 12-month prevalence of 0.8% (Gureje, Üstün, & Simon, 1997), whereas a study using cutoff scores from self-report measures followed by interviews suggests a 12-month prevalence of 8.5% (Noyes et al., 1993). The inclusion of the *with predominant pain* specifier to somatic symptom disorder, which subsumes a portion of the *DSM-IV* pain disorder diagnosis, may increase the prevalence of somatic symptom disorder beyond the prevalence of hypochondriasis.

The prevalence of illness anxiety disorder is relatively unknown, but can be estimated based on other phenomena. The 1- to 2-year prevalence of health anxiety and disease conviction (i.e., the belief that one has a disease) in community-based samples ranges from 1.3% to 10% (APA, 2013). A strong fear of contracting a disease, which is relatively similar to illness anxiety disorder, has a point prevalence of approximately 3% to 4% (Agras, Sylvester, & Oliveau, 1969; Malis, Hartz, Doebbeling, & Noyes, 2002). Together these findings suggest that illness anxiety disorder is relatively common.

The point and 12-month prevalence rates of conversion disorder in the general population are less than 0.1% (Akagi & House, 2001). Point prevalence in neurology and primary care settings has been reported as 1% (Smith, Clarke, Handrinos, Dunsis, & McKenzie, 2000) and 0.2% (de Waal, Arnold, Eekhof, & van Hemert, 2004), respectively. Despite low prevalence of conversion disorder, medically unexplained neurological symptoms are present in approximately 11% to 35% of neurology patients (Carson et al., 2000; Snijders, de Leeuw, Klumpers, Kappelle, & van Gijn, 2004), suggesting that subsyndromal conversion may be more common than almost all neurological diseases.

The prevalence of other somatic symptom and related disorders are unknown, partially because they are new diagnoses (e.g., psychological factors affecting other medical conditions) and are very difficult to study (e.g., factitious disorder, unspecified somatic symptom and related disorder).

PSYCHOLOGICAL AND BIOLOGICAL ASSESSMENT

Individuals with somatic symptom and related disorders will typically present in primary care and other medical (nonpsychiatric) clinics rather than in mental health settings; indeed, they may often refuse a mental health referral because of a belief that their condition is purely organic. Cooperation between medical and mental health professionals aids the referral process and, due to the complexity of the factors involved (e.g., possibility of co-occurring organic pathology), is typically necessary in making an accurate diagnosis. Throughout the course of assessing a person with a possible somatic symptom and related disorder, the mental health professional must seek to establish and maintain rapport and should clearly relay an understanding that, although a disease process may or may not be present, the symptoms are real and not feigned or "in the head" (Taylor & Asmundson, 2004). The general goals of assessment for the somatic symptom and related disorders are to rule out organic pathology-based, substance-based, or other psychopathology-based explanations of presenting signs and symptoms, to determine the type and severity of signs and symptoms, and to facilitate appropriate treatment planning.

Ruling out organic pathology is no longer requisite to diagnosis of somatic symptom and related disorders, as it was in the *DSM-IV-TR* somatoform disorders. This aspect of the diagnostic process was considered problematic for two primary reasons. First, it relied heavily on the exclusion of general medical conditions, and 100% certainty was rarely if ever possible (Taylor & Asmundson, 2004; Woolfolk & Allen, 2007). Second, diagnosis is not usually based on the absence of something but, rather, according to the presence of positive features of a condition (Dimsdale et al., 2013). Gathering a detailed history of somatic complaints, past and current medical conditions, and medical professionals consulted is a crucial part of a comprehensive diagnostic process and may provide insight regarding the nature of the presenting condition. A consult with the family physician may be necessary to determine the need for further medical assessments; however, caution is warranted, because further assessments may reinforce maladaptive coping (e.g., reassurance seeking) while also increasing the costs and potential risks associated with medical care.

Structured clinical interviews have proven to be the gold standard in the diagnosis of mental disorders, including somatoform disorders, and will likely remain so for the somatic symptom and related disorders. Broad structured interviews that include sections on numerous mental disorders are the most commonly utilized. The Structured Clinical Interview for the *DSM-IV* (First, Spitzer, Gibbon, & Williams, 1996) and the Composite International Diagnostic Interview (CIDI; World Health Organization, 1990) based on the *International Statistical Classification of Diseases*, 10th edition, criteria (*ICD-10*; World Health Organization, 2007) were both used widely and demonstrated efficacy and reliability in diagnosing somatoform disorders. Other useful structured interviews for diagnosing somatoform disorders included the Somatoform Disorders Schedule (World Health Organization, 1994), the Schedules for Clinical Assessment in Neuropsychiatry (Wing et al., 1990), and the Diagnostic Interview Schedule (Robins, Helzer, Croughan, & Ratcliff, 1981). At the time of writing this chapter, no revisions of these structured diagnostic interviews specific to the *DSM-5* criteria for the somatic symptom and related disorders had been released.

Structured clinical interviews can be supplemented with diarized monitoring of catastrophic thinking and maladaptive coping behaviors as well as information gleaned from standardized self-report measures. Self-report measures are efficient and effective screening tools that can provide invaluable information for case conceptualization and regular monitoring of treatment progress. The Screening for Somatoform Symptoms (Rief, Hiller, & Heuser, 1997), the Symptom Checklist–90, Revised (Derogatis, 1975), or the Patient Health Questionnaire–15 (Kroenke, Spitzer, & Williams, 2002) have been used to assess a broad range of somatic symptoms. More specific information can be derived from a wide array of self-report measures that have been developed to assess the severity of specific somatic symptoms. It is beyond the scope of this chapter to provide a comprehensive list of these measures; examples include the Health Attitude Survey (Noyes, Langbehn, Happel, Sieren, & Muller, 1999) for use in assessing attitudes and perceptions associated with multiple somatic symptoms, the Health Anxiety Questionnaire (Lucock & Morley, 1996) for use in assessing reassurance-seeking behavior and the extent to which symptoms interfere with a person's life, and the Whiteley Index (Pilowsky, 1967) for use in assessing cognitions associated with health anxiety. Whether such measures, or revisions thereof, prove to be of continuing value in the context of the *DSM-5* somatic symptom and related disorders remains to be determined. Medical service utilization and visual analogue scales pertaining to distressing thoughts and maladaptive coping behaviors can also be used to assess emotional and functional impact and to monitor treatment progress. Finally, measures of mood and anxiety can be useful in case conceptualization and monitoring and might include the Beck Depression Inventory–II (Beck, Steer, & Brown, 1996), the Beck Anxiety Inventory (Beck & Steer, 1993), and the original or recent 18-item expanded version of the Anxiety Sensitivity Index (Peterson & Reiss, 1987; Taylor et al., 2007).

ETIOLOGICAL CONSIDERATIONS

Behavioral Genetics and Molecular Genetics

Heritability of somatoform disorders has been suggested by findings from behavioral (e.g., Kendler et al., 2011; Torgersen, 1986) and molecular (e.g., Hennings, Zill, & Rief, 2009) genetics studies. Somatic symptom concordance rates between monozygotic twins are higher than between dizygotic twins, even when controlling for co-occurring psychiatric symptoms (Lembo, Zaman, Krueger, Tomenson, & Creed, 2009). Although mood and somatoform disorders share common genetic factors (e.g., deregulation of serotonergic pathways), there are numerous genetic features unique to somatoform disorders (e.g., immunological deregulation, hypothalamic-pituitary-adrenal [HPA] axis responses; Rief, Hennings, Riemer, & Euteneuer, 2010). The role of specific genetic markers in the development of somatic symptoms remains unclear; however, research in this area is ongoing, and genetic factors are now being considered within the context of psychological models of various somatoform disorders (e.g., Taylor, Jang, Stein, & Asmundson, 2008; Veale, 2004). Whether these findings generalize to the somatic symptom and related disorders remains to be determined.

Neuroanatomy and Neurobiology

Neurological research on the *DSM*-5 somatic symptom and related disorders remains in its infancy; but, research using *DSM-IV-TR* criteria has demonstrated neurological correlates for conversion disorder (e.g., Vuilleumier, 2005), hypochondriasis (e.g., Atmaca, Sec, Yildirim, Kayali, & Korkmaz, 2010), and other related disorders (e.g., somatization disorder, Hakala, Vahlberg, Niemi, & Karlsson, 2006; pain disorder and fibromyalgia, Wood, Glabus, Simpson, & Patterson, 2009). The HPA axis has been a focus of research in this area. A recent longitudinal study reported preliminary evidence that cortisol deregulation in the HPA axis may predate the development of somatic symptoms in some people (Tak & Rosmalen, 2010). The HPA axis controls glandular and hormonal responses to stress and, when stressors (e.g., chronic pain, anxiety) have a chronic course, may lead to hypocortisolism (i.e., adrenal insufficiency), which induces greater stress and enhances experiences of pain and fatigue (Fries, Hesse, Hellhammer, & Hellhammer, 2005). Increases in these experiences typically exacerbate somatic symptoms or lead to behaviors that exacerbate or maintain them (Taylor & Asmundson, 2004). The second somatosensory area (SII) of the cerebral cortex, which is involved in the analysis and evaluation of complex patterns of somesthetic input (e.g., perception of pain, sensations from visceral structures, gastric sensations), has also been implicated as a source of the somatic perturbation associated with the somatoform disorders (Miller, 1984); however, despite its appeal as a neural structure underlying this class of disorders, people presenting with concerns about somatic symptoms do not typically show abnormalities in sensory acuity.

Learning, Modeling, and Life Events

Childhood physical and sexual abuse and neglect have been associated with increased physician visits during adulthood (Fiddler, Jackson, Kapur, Wells, & Creed, 2004) and with hypochondriasis (Barsky, Wool, Barnett, & Cleary, 1994), as have other stressful life events unrelated to disease; however, it is noteworthy that increased prevalence of abuse and other stressful life events are characteristic of people with a variety of psychiatric conditions (e.g., panic disorder; Taylor, 2000), not just those presenting with concerns regarding somatic symptoms.

Early childhood experiences of illness and perceptions of significant illness in others are associated with the experience of medically unexplained symptoms in adulthood (Hotopf, Wilson-Jones, Mayou, Wadsworth, & Wessely, 2000). Likewise, parents who fear disease, who are preoccupied with their bodies, and who overreact to minor ailments experienced by their children are more likely to have children with the same tendencies, both during childhood and adulthood (Craig, Boardman, Mills, Daly-Jones, & Drake, 1993; Hotopf, Mayou, Wadsworth, & Wessely, 1999; Marshall, Jones, Ramchandani, Stein, & Bass, 2007). That being said, a recent twin study suggests that environmental factors not shared by twins (e.g., an ailment in one of the twins), rather than shared environmental factors (e.g., parental style), seem most important in the development of *DSM-IV-TR* defined hypochondriasis (Taylor & Asmundson, 2012).

Cognitive Influences

Greater focus on somatic sensations is associated with greater experiences of those sensations (Brown, 2004; Ursin, 2005). When attention is directed to the body, the intensity of perceived sensations increases (Mechanic, 1983; Pennebaker, 1980). People with somatoform disorders have been shown to spend a considerable amount of time focusing on their bodies, thereby increasing their chances of noticing somatic sensations and changes. They also tend to believe that somatic sensations and changes are indicative of disease or are otherwise harmful in some way (Barsky, 1992; Taylor & Asmundson, 2004; Vervoort, Goubert, Eccleston, Bijttebier, & Crombez, 2006). These beliefs increase the attention directed to somatic sensations and changes and, in turn, increase associated distress. It is likely that similar cognitive influences will be identified in the various somatic symptom and related disorders diagnoses.

Sex and Racial-Ethnic Considerations

As noted in the Epidemiology section, the somatoform disorders were more prevalent in women than in men, perhaps with the exception of hypochondriasis. There are several possible explanations for this difference. Because women are more likely to seek medical services (Corney, 1990; Kessler et al., 2008), they may be more prone to diagnostic biases wherein physicians consider somatic symptoms presented by a woman as more likely to be psychological than organic in nature (e.g., Martin, Gordon, & Lounsbury, 1998). Women also tend to experience higher rates of psychopathology (Kessler et al., 2008). Shared etiological or maintenance factors between mental disorders may make it more likely that women are at a higher risk of developing a somatic symptom and related disorder. There is evidence that women tend to focus more on their bodies (Beebe, 1995) and are more fearful of some of their bodily sensations (Stewart, Taylor, & Baker, 1997), further increasing their risk for developing somatic symptom and related disorders. Other putative sex differences have been proposed (e.g., differential experiences of abuse; HPA axis dysregulation) but warrant further empirical scrutiny in the context of their role in somatic symptom and related disorders etiology.

Somatic sensations and changes are common in all cultural groups; however, presentation varies widely depending on sociocultural norms (Kirmayer & Young, 1998). Cultural factors, such as socially transmitted values, beliefs, and expectations, can influence how a person interprets somatic sensations and changes, and whether treatment seeking is initiated. Some cultures appear to be more distressed by gastrointestinal sensations (e.g., excessive concerns about constipation in the United Kingdom), whereas others are more distressed by cardiopulmonary (e.g., excessive concerns about low blood pressure in Germany) and immunologically based (e.g., excessive concerns about viruses and their effects in the United States and Canada) symptoms (Escobar, Allen, Hoyos Nervi, & Gara, 2001). Whether one seeks care for somatic concerns also appears to vary as a function of culture, with those of Chinese, African American, Puerto Rican, and other Latin American descent presenting with more medically unexplained somatic symptoms than those from other groups (Escobar et al., 2001). Whether concern over somatic sensations and changes are excessive needs to be judged in the context of the individual's cultural background.

COURSE AND PROGNOSIS (INCLUDING ISSUES OF TREATMENT)

As a diagnostic category, somatic symptom and related disorders share somatic features and concerns as a prominent aspect of clinical presentation. That said, each disorder does not necessarily share a similar course and prognosis. Like the somatoform disorders, course and prognosis may vary considerably, because the disorders are heterogeneous in presentation and involve substantial comorbidity with mood and anxiety disorders, personality disorders, and, in some cases, general medical conditions. Certain prognostic indicators have been shown to be common across somatoform disorders; for example, comorbidity with other psychiatric disorders contributes to a more chronic and persistent course (e.g., Rief, Hiller, Geissner, & Fichter, 1995). More somatic symptoms, sensitization to bodily sensations and pain, as well as presence of a medical condition all contribute to greater severity and chronic course (APA, 2013). The presence of fewer somatic symptoms, few or no comorbid conditions, identifiable stressors at the time of onset, high intellectual functioning, as well as sound social support networks are typically associated with good prognosis. Also indicative of good prognosis is the development of a strong therapeutic alliance between the patient and care provider, wherein the patient believes that the care provider views the patient's presenting signs and symptoms as legitimate, albeit possibly not due to an organic pathology or physical defect (Taylor & Asmundson, 2004).

Research on psychological interventions does not yet exist for somatic symptom disorders; but, psychosocial interventions have demonstrated efficacy across the *DSM-IV-TR* somatoform disorders. Cognitive behavior therapy (CBT) has demonstrated to be superior to standard medical care in reducing health-related anxiety (Barsky & Ahern, 2004) and improving somatic complaints/somatization (Allen, Woolfolk, Escobar, Gara, & Hamer, 2006; Speckens, van Hemert, Bolk, Rooijmans, & Hengeveld, 1996). Psychiatric consultation letters to primary-care physicians describing somatization and providing recommendations for primary care have also been shown to significantly improve physical functioning and reduce cost of medical care (Rost, Kashner, & Smith, 1994). Similar interventions will likely prove effective with the somatic symptom and related disorders.

CASE STUDY

Case Identification

The basic features of this case are undisguised; however, in line with Clifft's (1986) guidelines, identifying information has been altered or omitted to protect confidentiality and privacy.

Jacob is a 37-year-old Caucasian male who has been married for 10 years and has a 5-year-old daughter and a 6-month-old son. He currently resides with his wife and children in an upper-middle-class suburban neighborhood. His family is financially secure, and he is not involved in any legal proceedings. Jacob is employed full time as an electrical engineer for a large company, a job he has held for the past 6 years. He enjoys a variety of sports, walking the family dog, and spending time with his family. Until recently, he was active as a competitive triathlete. His job requires that he travel periodically, with absences from home and his family for up to 1 month at a time. He

reports that job demands increase in the months prior to extended travel and that his next lengthy trip is fast approaching in 10 weeks.

Presenting Complaints

Jacob was referred by his family physician for assessment and, if appropriate, treatment of increasing anxiety over his physical well-being that was negatively impacting on his work (e.g., spending excessive amounts of time searching medical information on the Internet instead of working) as well as leisure and family functioning (e.g., withdrawing from physical activity and shared leisure activities). These concerns started 9 months ago, when his father died of heart complications associated with amyloidosis, a disease wherein amyloid proteins build up in specific organs and, over time, disrupt organ function and eventually lead to failure of the affected organs. There is a rare form—hereditary amyloidosis—that is most frequently passed from father to son and for which there are no preventive measures other than not having children. There is no cure for amyloidosis, and the effects do not become apparent until later in life (i.e., over the age of 50 years). Beginning shortly after his father's death, Jacob became increasingly aware of and concerned by somatic sensations in his body—heart palpitations and racing, upper body aches and pain, dizziness, and blurred vision—all of which were similar to those initially experienced by his father. He feared that he may also have amyloidosis and might die from it. His fears were exacerbated upon the birth of his son, with specific concerns that he had passed on the condition and that his son would eventually succumb as well.

History

Jacob had no prior history of mental health problems or treatment and, aside from chicken pox and tonsillitis as a child, had been physically healthy throughout his life. The report from his physician indicated that, despite numerous visits regarding various somatic complaints over the past months, there was no evidence of an organic basis for Jacob's concerns. The physician report also indicated that Jacob was physically healthy and that he and his son had a pending appointment for genetic testing to rule out the genetic profile for hereditary amyloidosis. Jacob reported having a loving and supportive relationship with his wife, although she was becoming increasingly concerned by his condition and, at times, annoyed at his growing reluctance to actively play with their children. Until recently, he was exercising five or six times per week and had competed in numerous triathlons; however, because of growing concerns about his health, he had significantly cut down his frequency of training and was not competing in order to "avoid physical exertion" for fear that his heart would "explode." In place of training, he was spending hours checking the Internet for medical information.

Assessment (Related to *DSM-5* Criteria)

Jacob was assessed using a semistructured interview that included probes pertinent to the diagnostic criteria for *DSM-5* somatic symptom and related disorders and a battery of self-report questionnaires. The former was drafted for use in place of the Structured

Clinical Interview for the *DSM-5*, which was not yet available at time of assessment. The latter included (a) the Beck Depression Inventory–II, a measure of depression over the past 2 weeks (Beck et al., 1996), (b) the Beck Anxiety Inventory, a measure of general anxiety over the past week (Beck & Steer, 1993), (c) the Anxiety Sensitivity Index (Peterson & Reiss, 1987), a measure of the fear of arousal-related bodily sensations, and (d) the Whiteley Index (Pilowsky, 1967), a measure of the core features of health anxiety, including disease fear, disease conviction, and bodily preoccupation. The structured interview and self-report data provided detailed data regarding general features of Jacob's distress, as well as specific features of his health-related concerns.

Jacob met the *DSM-5* diagnostic criteria for somatic symptom disorder. He presented with several specific concerns, including daily worry that somatic changes and sensations (e.g., heart palpitations and racing, upper body aches and pain, dizziness, blurred vision) were signs of physical disease as well as increasing inability to focus on work-related tasks and to be involved in family activities (somatic symptom disorder Criterion A). He also presented with considerable worry and anxiety about his personal health and the future-oriented health and well-being of his 6-month-old son, and reported spending hours on the Internet checking medical information (somatic symptom disorder Criterion B). His concerns had, as noted previously, begun around the time of his father's death 9 months prior and had persisted since (somatic symptom disorder Criterion C).

Given that the effects of amyloidosis are typically not evident until later in life, and that Jacob was in his mid-30s, it was deemed unlikely that amyloid deposits were responsible for the bodily sensations he was experiencing; however, since Jacob (and his son) had not yet completed genetic testing and did not know whether they had the genetic profile for hereditary amyloidosis at the time of assessment, we remained cautious in our opinion whether his thoughts about the seriousness of symptoms were disproportionate. At the time of assessment, Jacob's score on the Whiteley Index was moderate overall (score = 8; possible range 0–14), characterized by significant disease fear (score = 3; possible range 0–4) and bodily preoccupation (score = 3; possible range 0–3) but little disease conviction (score = 0; possible range 0–3), the latter of which is indicative of good prognosis with treatment (Taylor & Asmundson, 2004). The moderately high levels of health anxiety combined with excessive checking behavior, in our opinion, were sufficient to warrant a moderate severity specifier.

Jacob did not meet diagnostic criteria for other diagnosis. Scores on the Beck Depression Inventory (score = 13; possible range 0–63) and Beck Anxiety Inventory (score = 26; possible range 0–63) suggested a mildly depressed mood and moderate general anxiety, respectively. The absence of comorbid diagnoses, along with depression and general anxiety in the mild to moderate range, are also indicative of good prognosis with treatment (Taylor & Asmundson, 2004). His score on the Anxiety Sensitivity Index (score = 26; possible range 0–64) indicated strong beliefs that arousal-related bodily sensations have harmful consequences, which, when considered in the context of his significant disease fear and bodily preoccupation, suggest that attention-focusing exercises (e.g., Furer, Walker, & Stein, 2007; Wells, 1997) and interoceptive exposure (Taylor & Asmundson, 2004) may prove to be particularly beneficial additions to treatment.

SUMMARY

Conditions characterized by significant concern over somatic signs and symptoms, often presenting as medically unexplainable, are associated with significant emotional distress, cognitions characterized by catastrophic thinking, maladaptive coping behaviors typically manifest as excessive checking and reassurance seeking, limitations in social and occupational functioning, and excessive use of health care resources. These conditions are represented by the disorders subsumed under the current *DSM-5* somatic symptom and related disorders. It remains to be determined whether the changes from the *DSM-IV-TR* somatoform disorder to the *DSM-5* somatic symptom and related disorders will promote more accurate diagnosis of people concerned and functionally disabled by somatic sensations and changes and, if so, whether this will direct appropriate treatment resources to optimize outcomes. It also remains unclear if, or how, the changes to classification will facilitate efforts to identify underlying mechanisms. The burden on the health-care system and the personal distress associated with somatic symptoms highlight the need for appropriate reconceptualization of disorders characterized by somatic symptom presentation; however, some investigators have suggested that there was insufficient empirical evidence to warrant change, that important evidence may have been overlooked, and that the changes in the *DSM-5* may have been premature (Taylor, 2009; Sirri & Fava, 2013; Starcevic, 2013), and that the new changes will increase, rather than decrease, diagnostic misclassification (Frances, 2013). Answers to these questions await the accumulation of empirical evidence based on the new *DSM-5* diagnostic criteria.

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CHAPTER 13

Feeding and Eating Disorders

CYNTHIA M. BULIK, SARA E. TRACE, SUSAN C. KLEIMAN, and SUZANNE E. MAZZEO

DESCRIPTION OF THE DISORDERS

Eating disorders represent a category of partially overlapping syndromes, all of which have some clinical features marked by eating dysregulation. We will focus our discussion on anorexia nervosa (AN), bulimia nervosa (BN), and binge eating disorder (BED), which represent the primary eating disorders listed in *DSM-5*. Feeding disorders, such as pica, rumination disorder, and avoidant/restrictive food intake disorder—all more common in, but not exclusive to children—will not be covered here. Eating disorders are serious mental illnesses that are influenced by both genetic and environmental factors. The syndromes are partially overlapping, as considerable diagnostic flux occurs over time, with individuals migrating from one clinical presentation to another, and because several diagnostic features are shared across disorders. Nonetheless, pure forms of each of the presentations also exist.

CLINICAL PICTURE

AN, the most visible eating disorder, is a serious psychiatric illness characterized by an inability to maintain a normal healthy body weight or, in individuals who are still growing, failure to make expected increases in weight (and often height) and bone density. Despite increasing weight loss and frank emaciation, individuals with AN strive for additional weight loss, see themselves as fat even when they are severely underweight, and often engage in unhealthy weight-loss behaviors (e.g., purging, dieting, excessive exercise, and fasting).

AN is characterized by low weight; however, how one defines low weight is somewhat complicated. *DSM-5* highlights restriction of energy intake relative to requirements, leading to a significantly low body weight, and embeds that in the context of the individual's age, sex, developmental trajectory, and physical health. Even when at low weight, people with AN experience an intense fear of gaining weight or of becoming fat, or they engage in persistent behavior that interferes with weight gain. The behavior and cognitions of individuals with AN vigorously defend low body weight. Other aspects of the diagnostic criteria include a three-part criterion of which only one component is necessary: disturbance in the way in which one's body

weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight.

In the past, amenorrhea of 3 months or longer duration was a diagnostic criterion for AN. Wisely, this has been eliminated, as there are no meaningful differences between individuals with AN who do and do not menstruate (Gendall et al., 2006; Watson & Andersen, 2003). Although not diagnostic, cessation of menstruation can be a useful indicator of severity and resumption of menses a factor in determining recovery. AN presents either as the restricting subtype, in which low weight is achieved and maintained through energy restriction and increased physical activity only, or as the binge-eating/purging subtype, in which the individual has been regularly engaging in binge eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas) over the past 3 months.

BN is characterized by recurrent binge eating episodes, defined as eating an unusually large amount of food in a short period of time (~2 hours) while experiencing a sense of loss of control over the eating episode. In addition, bulimia includes recurrent inappropriate compensatory behaviors (e.g., self-induced vomiting, laxative, diuretic, or other medication misuse, fasting, or excessive exercise). In individuals with BN, self-evaluation is unduly influenced by body shape and weight. Binge eating and compensatory episodes occur on average once a week for at least 3 months. BN is only diagnosed if AN criteria are not met. Thus, to be diagnosed with BN, individuals should have a body mass index (BMI) greater than 18.5 kg/m^2 in adults (i.e., the lower bound of normal weight according to the World Health Organization [1992] and the Centers for Disease Control).

BN onset most frequently occurs in adolescence or early adulthood, although it can occur at any point across the life span (American Psychiatric Association [APA], 2013). BN can occur at any body weight (with the exception of the requirement to diagnose AN binge-eating/purging type if criteria for AN are met). BN tends to be overrepresented in women; however, it has been argued that BN diagnostic criteria are gender-biased, leading to underdetection in men. Men who seek treatment for BN tend to manifest a greater reliance on nonpurging forms of compensatory behavior, such as excessive exercise (Anderson & Bulik, 2003; Lewinsohn, Seeley, Moerk, & Striegel-Moore, 2002). It is important to consider such gender differences in the clinical presentation of BN to revise prevalence estimates of this diagnosis (Anderson & Bulik, 2003).

In *DSM-5*, BED finally received recognition as a stand-alone disorder after years of being categorized as a disorder "worthy of further study." Binge eating was first noted in a subset of obese individuals by Stunkard in 1959 (Stunkard, 1959). BED has had a slow and controversial evolution in the psychiatric nosology for eating disorders (Fairburn, Welch, & Hay, 1993; Spitzer et al., 1993; Walsh, 1992).

BED is marked by recurrent binge eating (at least weekly for 3 months, as in BN) and a sense of lack of control over eating during the episode, but in the absence of regular compensatory behaviors. Unlike BN, the diagnostic criteria for BED include descriptions of the binge experience. To meet criteria, an individual must experience distress regarding the binge eating and at least three of the following: eating much more rapidly than normal, eating until feeling uncomfortably full, eating large amounts of food when not feeling physically hungry, eating alone because of feeling

embarrassed by how much one is eating, or feeling disgusted with oneself, depressed, or very guilty afterward. It remains a curiosity why these descriptors remained in the BED criteria when they are not in the BN criteria; presumably, this was related to ensuring that individuals who simply overeat were not misdiagnosed as having BED. BED can occur at any body weight and is only diagnosed if neither AN nor BN criteria are met.

Other Specified Feeding or Eating Disorder (OSFED) is a new category in *DSM-5*, which replaces the historical Eating Disorder Not Otherwise Specified (EDNOS). The reorganization in *DSM-5* occurred in part because BED became a stand-alone diagnosis and in part because, historically, far too many individuals with eating disorders received a diagnosis of EDNOS, rendering it the most frequently diagnosed eating disorder. This alerted many researchers and clinicians to the fact that the diagnostic system was in need of revision so that a greater number of individuals could be captured under the hallmark categories of AN, BN, and BED. OSFED applies to presentations with symptoms characteristic of a feeding and eating disorder but to presentation where full diagnostic criteria are not met. Given that this is indeed a new category, we have very little epidemiologic data that reflect the new diagnosis. Research over the next several years will reveal how the transformation of the diagnostic schema has reshuffled the prevalences of the various disorders.

OSFED includes a useful category of atypical AN, in which an individual meets all criteria for AN except that their weight falls within or above the normal weight range. This would capture, for example, an individual who was obese who precipitously lost a large amount of weight and exhibited all of the psychological features of AN, but because of the weight at which the weight loss started, still fell in the normal weight range. Other presentations under OSFED include BN and BED of low frequency or limited duration, purging disorder (which is purging behavior in the absence of binge eating), and night eating syndrome, in which individuals report recurrent episodes of night eating, marked by eating after awakening from sleep or by excessive food consumption after the evening meal.

Based on previous research with EDNOS, what we do not expect to change is that being in the OSFED category in no way implies that an individual has a less serious disorder. The severity of pathology and psychosocial impairment is comparable among individuals with EDNOS, AN, and BN (Fairburn & Bohn, 2005; Keel, Gravener, Joiner, & Haedt, 2010). Clinical descriptions of EDNOS are consistent in stating that most cases have features similar to AN and BN (Crow, Agras, Halmi, Mitchell, & Kraemer, 2002; Waller, 1993; Walsh & Garner, 1997). Three studies (Fairburn & Cooper, 2007; Ricca et al., 2001; Turner & Bryant-Waugh, 2003) using the Eating Disorder Examination (EDE; Cooper & Fairburn, 1987) found that individuals with EDNOS presented with significant cognitive symptomatology related to eating, shape, and weight, suggesting that these syndromes are clinically significant.

DIAGNOSTIC CONSIDERATIONS

With the publication of *DSM-5* in 2013, investigation of the validity of the new classification system is an important research focus. Some advances of the *DSM-5* system include attention to stages of illness. In the past, for example, if someone had met criteria for AN and then began to recover, she or he might have received a new

diagnosis of EDNOS. In *DSM-5*, there is now the option to include the specifier of "in partial remission" if, after having met full criteria, weight has normalized but the psychological features remain, and "full remission" if, after having met full criteria, no criteria have been met for a sustained period of time. In addition, severity specifiers also exist, and are currently based on body mass index (BMI), with mild AN being ≥ 17 kg/m^2, moderate 16–16.99 kg/m^2, severe 15–15.99 kg/m^2, and extreme <15 kg/m^2.

In addition to the core diagnostic features, individuals with AN often manifest a specific cluster of personality traits, including perfectionism, obsessionality, anxiety, harm avoidance, and low self-esteem (Cassin & von Ranson, 2005; Fassino, Amianto, Gramaglia, Facchini, & Abbate Daga, 2004; Klump et al., 2000). Furthermore, both these personality characteristics and anxiety disorders often precede AN onset (Bulik, Sullivan, Fear, & Joyce, 1997; Kaye et al., 2004). Major depression and anxiety disorders frequently co-occur with AN (Bulik et al., 1997; Fernandez-Aranda et al., 2007; Godart, Flament, Perdereau, & Jeammet, 2002; Godart, Flament, Lecrubier, & Jeammet, 2000; Kaye et al., 2004), and longitudinal research suggests that depression often persists following recovery from AN (Sullivan, Bulik, Fear, & Pickering, 1998).

Some personality features common among individuals with AN are also manifested by many women with BN, such as high harm avoidance, perfectionism, and low self-esteem. However, other personality features appear more specific to BN, including elevated novelty seeking and impulsivity, low self-directedness, and low cooperativeness (Bulik, Sullivan, Carter, & Joyce, 1995; Fassino et al., 2004; Steiger et al., 2004). Further refinements of the components of impulsivity suggest that negative urgency, or the tendency to act rashly when distressed, is the facet of impulsivity most strongly associated with bulimia (Fischer, Smith, & Cyders, 2008).

Comorbid psychiatric disorders are very common among individuals with BN, occurring among nearly 80% of patients (Fichter & Quadflieg, 1997). These comorbidities include anxiety disorders, major depression, dysthymia, substance use, and personality disorders (Braun, Sunday, & Halmi, 1994; Brewerton et al., 1995; Bulik et al., 2004; Perez, Joiner, & Lewinsohn, 2004).

Finally, BED also commonly co-occurs with numerous other psychiatric diagnoses, including mood, anxiety, and substance abuse disorders (Grucza & Beirut, 2007; Johnson, Spitzer, & Williams, 2001; Marcus, Wing, & Fairburn, 1995; Striegel-Moore et al., 2001; Wilfley, Freidman, et al., 2000). Data from the National Comorbidity Survey Replication (Hudson, Hiripi, Pope, & Kessler, 2007) indicate that BED is a chronic condition associated with significant impairment in daily functioning. Global data from the World Heath Organization World Mental Health Surveys indicate that BED and BN are associated with significantly increased education in women. Early-onset BED predicted reduced odds of marriage in women and reduced odds of employment in men, while early-onset BN predicted increased odds of current work disability in both sexes. Both BED and BN were associated with significantly increased days of role impairment, although much of the role impairment was accounted for by the presence of comorbid disorders (Kessler, Shahly, et al., 2013).

Finally, those individuals with BED who are overweight or obese are at risk for medical complications (Hudson et al., 2007). Yet, the negative psychological impact of BED does not appear to be attributable to obesity. Obese individuals with BED report substantially poorer psychological functioning than do obese individuals without BED (Grucza, Przybeck, & Cloninger, 2007), and normal weight and overweight

individuals with BED report equivalent psychological features of disordered eating and depression (Dingemans & van Furth, 2012).

EPIDEMIOLOGY

Available epidemiologic data on eating disorders reflect *DSM-IV* diagnostic criteria, because sufficient time has not yet elapsed for studies to be conducted on the new classifications. Lifetime prevalence estimates of *DSM-IV* AN, BN, and BED from a nationally representative population sample over age 18 are 0.9%, 1.5%, and 3.5% in women, and 0.3%, 0.5%, and 2.0% in men, respectively (Hudson et al., 2007). The prevalence of subthreshold AN, defined as at least one criterion short of threshold, is greater and ranges from 0.37% to 1.3% (Hoek, 1991). The gender ratio for AN is approximately 9:1, women to men (APA, 1994). Awareness of these disorders has increased; however, the data on changing incidence are conflicting. Some studies report increasing incidence of AN or increases in disordered eating behavior (such as strict dieting or fasting for weight or shape control) that are associated with AN (e.g., Hay, Mond, Buttner, & Darby, 2008; Lucas, Crowson, O'Fallon, & Melton, 1999; Eagles, Johnston, Hunter, Lobban, & Millar, 1995; Jones, Fox, Babigan, & Hutton, 1980; Møller-Madsen & Nystrup, 1992), whereas others describe stable prevalence (e.g., Smink, van Hoeken, & Hoek, 2012; Hoek, 2006; Currin, Schmidt, Treasure, & Jick, 2005; Pawluck & Gorey, 1998; Hall & Hay, 1991; Hoek et al., 1995). The peak age of onset for AN is between 15 and 19 years (Lucas, Beard, O'Fallon, & Kurland, 1988), an age group for which incidence has been increasing (Smink et al., 2012). However, reports suggest new-onset cases in mid- and late life (Gagne et al., 2012; Mangweth-Matzek et al., 2006; Beck, Casper, & Andersen, 1996; Inagaki et al., 2002) and increasing presentations in children (Rosen, 2010).

The prevalence of BN in the United States is estimated to be 1.5% for women and 0.5% for men (Hudson et al., 2007). The prevalence of subthreshold behaviors is considerably higher, with 4.9% of women and 4% of men endorsing any binge eating. Similar to AN, reports suggest that more children and older adults are presenting with BN (Marcus et al., 2007; Rosen, 2010).

The prevalence of BED in the United States has been estimated at 3.5% for women and 2% for men (Hudson et al., 2007), while community surveys across 12 countries estimate the lifetime prevalence across both genders at 1.9% (Kessler, Shahly, et al., 2013). In a population-based study of female twins, 37% of obese women (BMI $\geq$ 30) reported binge eating (Bulik, Sullivan, & Kendler, 2002), representing 2.7% of the female population studied. Community studies of obese individuals have found a prevalence of BED between 5% and 8% (Bruce & Agras, 1992; Bruce & Wilfley, 1996). The sex distribution in BED is more equal than in AN or BN (Hudson et al., 2007) with few differences in prevalence across races or ethnic groups (Alegria et al., 2007; Marcus et al., 2007).

PSYCHOLOGICAL AND BIOLOGICAL ASSESSMENT

Careful and accurate assessment of eating disorders, which are frequently complex and have multiple presentations, is critical for effective treatment and research. The general goal of psychological assessment is to elicit information that accurately

describes symptomatology, accurately characterizes diagnostic profile, and indicates appropriate treatment recommendations (Peterson & Mitchell, 2005). Assessing individuals with eating disorders is often challenging secondary to denial of the illness and hidden signs and symptoms (Palmer, 2003; Schacter, 1999; Tury, Gulec, & Kohls, 2010; Vitousek, Daly, & Heiser, 1991). The use of active listening skills is important for developing rapport (Keel, 2001), and motivational interviewing techniques (Miller & Rollnick, 2002), which encourage rolling with resistance, avoiding arguments, and expressing empathy, are often helpful for conducting a successful assessment.

Clinical interviews in eating disorders are used to elicit the patient's perspective of the development of his or her difficulties and frequently include the reason for the assessment/primary complaint, history of present illness, medical complications, treatment history, and coexisting conditions (Peterson, 2005). A combination of structured interviews, self-report measures, and medical assessments may also be employed to obtain a more complete clinical picture. In the case of minors, corroborating information, such as reports from parents or school officials, is additionally informative (Lock, Le Grange, Agras, & Dare, 2001).

STRUCTURED INTERVIEWS

Structured interviews are essential for clarifying differential diagnostic issues and assessing psychiatric comorbidity. Structured interviews are advantageous in that they allow for active involvement of the interviewer, who can help clarify concepts or answer questions that may arise during the assessment. Obvious drawbacks to structured interviews include greater financial cost and clinician burden (Grilo, 2005).

For untrained interviewers, the two dominant instruments for assessing Axis I pathology are the Diagnostic Interview Schedule (DIS; Robins, Helzer, Croughan, & Ratcliff, 1981) and the Composite International Diagnostic Interview (CIDI; World Health Organization, 1990). The various versions of the Structured Clinical Interview for *DSM-IV* (SCID; First, Spitzer, Gibbon, & Williams, 2002), which has excellent validity and reliability (Grilo, 2005; Zanarini et al., 2000), are recommended for assessing Axis I pathology in adults by trained interviewers.

Several clinician-based structured or semistructured interviews have been developed specifically for assessing eating disorder symptomatology. The Eating Disorder Examination (EDE; Cooper & Fairburn, 1987) is well-established (Wilfley, Schwartz, Spurrell, & Fairburn, 2000) and widely used. It includes 33 items that measure behavioral and psychological traits in AN and BN and, with the exception of the diagnostic items, focuses on the 28 days preceding the assessment. Items are rated on a 7-point Likert-type scale, with higher scores indicating greater pathology, and comprise the following scales: dietary restraint, eating concern, weight concern, and shape concern. The EDE has high interrater reliability (Cooper & Fairburn, 1987; Grilo, Masheb, Lozano-Blanco, & Barry, 2004; Rizvi, Peterson, Crow, & Agras, 2000), adequate internal consistency (Beumont, Kopec-Schrader, Talbot, & Touyz, 1993; Cooper, Cooper, & Fairburn, 1989), and good discriminative validity for distinguishing those with eating disorders from healthy individuals (Cooper et al., 1989; Wilson & Smith, 1989). Other popular structured interviews for assessing disordered eating include the Interview for Diagnosis of Eating Disorders (IDED; Williamson, 1990) and the Structured Interview for Anorexic and Bulimic Disorders (SIAB-EX; Fichter et al.,

1998). For a full review of these and other structured interviews in eating disorders, see Grilo, 2005.

The IDED-IV (Kutlesic, Williamson, Gleaves, Barbin, & Murphy-Eberenz, 1998) is another semistructured interview primarily used for differential diagnosis of *DSM-IV* AN, BN, and EDNOS. The IDED-IV differs from the EDE in that it does not focus on frequency and severity data, but rather on differential diagnosis. Four studies support the psychometric properties of this instrument (Kutlesic et al., 1998).

The current version of the SIAB-EX (Fichter et al., 1998) assesses specific criteria for AN and BN (including subtypes), consistent with both the *DSM-IV* and the *ICD-10*. There is also an algorithm that allows the data to be used to generate the BED research diagnosis and other eating disorder syndromes under the EDNOS category. The SIAB-EX has demonstrated good internal consistency, factor structure, interrater reliability, and convergent and discriminant construct validity (Fichter & Quadflieg, 2000, 2001). Overall, the EDE and the SIAB-EX have been shown to produce generally similar findings. However, areas of divergence do exist, many of which could be attributable to the differences in criteria and time frames for assessment (Fichter & Quadflieg, 2001).

Self-Reports

Many self-report measures are available for assessing disordered eating both in research and clinical settings. Self-report assessments can be used for a variety of purposes, including identifying clinical features, quantifying symptoms, and verifying diagnoses. They are particularly useful for assessing change over time and are time and cost effective because they can be completed independently by the patient (Peterson & Mitchell, 2005). Two of the most widely used self-report questionnaires for assessing disordered eating include the Eating Disorder Inventory (EDI) and the Eating Disorder Examination–Questionnaire (EDE-Q).

The EDI (Garner, Olmsted, & Polivy, 1983, 1984), which assesses eating disorder symptoms and associated psychological traits, is useful for differentiating levels of eating disorder severity and for assessing treatment outcome (Williamson, Anderson, Jackman, & Jackson, 1995). This assessment is described by the authors as "investigator-based," emphasizing that it is the investigator's job to make final judgments about what symptoms and behaviors are present (e.g., to determine what constitutes a binge). The EDI has 64 questions answered on a 6-point Likert-type scale and comprises the following eight subscales: drive for thinness, bulimia, body dissatisfaction, ineffectiveness, perfectionism, interpersonal distress, interoceptive awareness, and maturity fears. A revised version of the EDI, the EDI-2, was published in 1991 and includes 27 additional questions. The eight scales from the EDI were retained, and three additional scales—asceticism, impulse regulation, and social insecurity—were incorporated (Garner, 1991).

The third version of the scale, EDI-3 (Garner, 2004), retained the same items as the EDI-2 but has a slightly different factor structure (Garner, Olmsted, & Polivy, 2008). It contains 91 items rated on a 0–4 point scoring system. The three subscales assessing eating pathology added in the EDI-2 (drive for thinness, bulimia, and body dissatisfaction) remain largely unchanged, and the general psychology subscales include low self-esteem, personal alienation, interpersonal insecurity, interpersonal alienation,

interoceptive deficits, emotional dysregulation, perfectionism, asceticism, and maturity fears. Scoring for the EDI-3 includes the following six composite scores: (1) eating disorder risk, (2) ineffectiveness, (3) interpersonal problems, (4) affective problems, (5) over control, and (6) general psychological maladjustment, as well as infrequency and negative impression scores. The EDI-3 has yielded reliable and valid scores (Garner, 2004).

The EDE-Q (Fairburn & Beglin, 1994), another widely used self-report measure of eating disorder symptoms, assesses severity of eating pathology and associated disturbances over the past 28 days. It is most often used in research, but it can be applied in clinical settings as well (Peterson & Mitchell, 2005). The EDE-Q was adapted from the structured interview EDE (Cooper & Fairburn, 1987), and like the EDE, it consists of 33 items and four subscales (restraint, eating concern, shape concern, and weight concern). The subscales and total scores are based on averages from 0 to 6, with higher scores indicating greater pathology. The EDE-Q has been described as an accurate method for assessing binge eating (Wilson, Nonas, & Rosenbaum, 1993) and shows acceptable reliability and validity (Fairburn & Cooper, 1993).

There are numerous other self-report assessments for eating disorders, including the Multiaxial Assessment of Eating Disorder Symptoms (MAEDS; Anderson, Williamson, Duchmann, Gleaves, & Barbin, 1999), the Stirling Eating Disorder Scales (SEDS; Williams et al., 1994), the Anorexia Nervosa Inventory for Self-Rating (ANIS; Fichter & Keeser, 1980), the Three Factor Eating Questionnaire (TFEQ; Stunkard & Messick, 1985), the Binge Eating Scale (BES; Gormally, Black, Daston, & Rardin, 1982), and the Questionnaire for Eating and Weight Patterns-Revised (QEWP-R; Yanovski, 1993). A full review of these and other self-report measures for assessing disordered eating can be found in Peterson and Mitchell (2005) or Tury, Gulec, and Kohls (2010).

Medical Assessment

Careful medical assessment, both initially and as indicated throughout the duration of eating disorder treatment, is critical for effective treatment (Crow, 2005). It is also important for Emergency Medicine physicians to be able to screen for and recognize patients with eating disorders, and to be aware of their medical complications and psychiatric comorbidities, in order to carry out a successful therapeutic intervention (Trent, Moreira, Colwell, & Mehler, 2013; Mascolo, Trent, Colwell, & Mehler, 2012). Documentation of medical complications is imperative, not only for treatment planning but also for service authorization by insurance companies. Although all eating-disorder presentations require medical monitoring, low-weight patients, individuals with purging behaviors, and obese individuals with binge-eating behavior (or a combination of these behaviors) are typically at the greatest risk for medical complications (e.g., Crow, Salisbury, Crosby, & Mitchell, 1997; Harris & Barraclough, 1998; Kohn, Golden, & Shenker, 1998).

Low-weight individuals are particularly vulnerable to medical morbidity and mortality (Harris & Barraclough, 1998). A BMI below 13 is associated with less favorable outcome (Hebebrand et al., 1997), and low weight is associated with increased likelihood of sudden cardiac death. AN, BN, and EDNOS are all associated with increased mortality (Crow et al., 2009). Evidence of medical complications might also encourage otherwise resistant patients to enter treatment. A standard initial

assessment for low-weight individuals should include a complete blood count, an electrolyte battery (including phosphorus, calcium, and magnesium), an electrocardiogram, liver function tests, and a dual-energy X-ray absorptiometry (DEXA) scan (Crow, 2005). Blood pressure and pulse should also be documented, as dehydration can lead to orthostatic hypotension. The patient should be monitored carefully through the re-feeding process, because provision of adequate calories may lead to a drop in serum phosphorus, which is associated with mortality (Kohn et al., 1998) both in hospital (Ornstein, Golden, Jacobson, & Shenker, 2003) and outpatient settings (Winston & Wells, 2002).

Electrolyte disturbance is the most commonly recognized complication of purging behaviors (Crow et al., 1997). Although not sensitive to vomiting frequency, hypokalemia is a marker of vomiting behavior (Crow et al., 1997). Another common complication of self-induced vomiting is parotid hypertrophy, or painless swelling of the parotid glands, which may persist for months following cessation of purging (Ogren, Huerter, Pearson, Antonson, & Moore, 1987). Dental complications, including dental enamel erosion on the lingual surfaces of teeth (Little, 2002), may occur in individuals who vomit frequently and, thus, continued dental monitoring is important. A smaller number of individuals with purging behaviors report gastrointestinal symptoms, including intestinal bleeding, hematemesis (vomiting blood), the passing of melanotic stools, or blood in the stools. Although rare, esophageal tears, gastric erosions, hemorrhoids, and gastric rupture may also occur (Cuellar, Kaye, Hsu, & Van Thiel, 1988; Cuellar & Van Thiel, 1986). Abuse of laxatives and emetics are also associated with significant medical morbidity. The use of syrup of Ipecac should signal a medical and cardiac evaluation, as it is associated with severe cardiac effects.

BED, which is among the most common of eating disorder presentations, is often associated with co-occurring conditions (Crow, 2005), including Type II diabetes mellitus and obesity. There is some evidence to suggest that obese individuals with Type II diabetes mellitus who also binge eat experience worse outcomes than their non-binge-eating peers (Goodwin, Hoven, & Spitzer, 2003; Mannucci et al., 2002). Binge eating appears to be associated with medical problems independent of obesity (Bulik et al., 2002). Moreover, BED may confer a risk of developing metabolic syndrome (a cluster of related risk factors for atherosclerotic cardiovascular disease, including abdominal obesity, dyslipidemia, hypertension, and abnormal glucose metabolism) beyond the risk attributable to obesity alone (Hudson et al., 2010). It is critical to remember that not all individuals with BED are overweight or obese. We await further data on the health impact of BED in normal weight individuals.

The growing interest in eating disorders over the past 20 years has resulted in the development of numerous assessment tools for research and clinical purposes. Accurate assessment of individuals with disordered eating requires a multidisciplinary approach to address both the psychological and biological factors underlying etiology.

ETIOLOGICAL CONSIDERATIONS

Although numerous psychological, social, and biological factors have been implicated as potential causes of eating disorders, few specific risk factors have been consistently identified across studies, and the etiology of these disorders is not fully understood

(Jacobi, Hayward, de Zwaan, Kraemer, & Agras, 2004; Striegel-Moore & Bulik, 2007). Common risk factors across eating disorders include female sex, race, or ethnicity, childhood eating and gastrointestinal problems, elevated concerns about shape and weight, negative self-evaluation, prior history of sexual abuse and other adverse events, and presence of additional psychiatric diagnoses (Jacobi et al., 2004). Developmentally, prematurity, smallness for gestational age, and cephalohematoma have been identified as possible risk factors for AN (Cnattingius, Hultman, Dahl, & Sparen, 1999).

Current studies suggest that eating disorders are caused by a variety of factors, including both genetic (e.g., Trace, Baker, Peñas-Lledó, & Bulik, 2013; Bulik, Slof-Op't Landt, van Furth, & Sullivan, 2007) and environmental influences (e.g., Becker & Hamburg, 1996; Garner & Garfinkel, 1980; Striegel-Moore & Bulik, 2007). Contemporary understanding of eating disorders incorporates both genetic and environmental factors into causal models. Previously, an overemphasis on sociocultural factors ignored the fact that, although social pressures toward thinness are ubiquitous, only a fraction of individuals exposed to these factors develop eating disorders. Therefore, a clearer understanding of vulnerability has led to the model that individuals who are more genetically predisposed to eating disorders are those who are also more vulnerable to environmental triggers of illness—typically ones that result in dieting, drive for thinness, and persistent negative energy balance.

Environmental influences that might serve as eating disorder triggers include the media's idealization of the thin body ideal and pressure to achieve an unrealistically thin body type (Irving, 1990; Levine & Harrison, 2004). Sociocultural models of disordered eating (Polivy & Herman, 1985; Striegel-Moore, Silberstein, & Rodin, 1986) suggest that the perception of a discrepancy between the self and the thin ideal leads to psychological discomfort. In turn, a desire to ameliorate this discomfort might result in eating disordered behavior. Striegel-Moore and Bulik (2007) report that cultural models of eating disorders are supported by the following: (a) the high percentage of female cases of disordered eating; (b) the increase in incidence of eating disorders in women coinciding with the decreasing body-weight ideal for women; (c) the reported higher incidence of eating disorders in cultures that emphasize thinness; and (d) the significant association between thin ideal internalization and disordered eating.

In a community-based case-control study, Fairburn et al. (1998) found significant differences in exposure to risk factors between women with BED and healthy controls, but surprisingly few differences between women with BED and BN. Specifically, compared with controls, women with BED reported more adverse childhood experiences, parental depression, personal vulnerability to depression, and exposure to negative comments about weight, shape, and eating.

Other studies have indicated that environmental factors, including parental and peer behaviors, contribute to both risk and protection from eating pathology (Enten & Golan, 2009; Twamley & Davis, 1999). For example, Twamley and Davis reported that low family pressures to control weight moderated the relation between exposure to thin norms and internalization of these messages. In addition, other environmental variables, including social pressure, could amplify or mitigate the risk of eating disorders (Striegel-Moore et al., 1986). For example, individuals exposed to peer teasing might be more likely to develop disordered eating (Thompson, Coovert, Richards, Johnson, & Cattarin, 1995; Thompson & Heinberg, 1993). Similarly,

individuals from higher social classes might be more prone to develop disordered eating, as they presumably have more time, attention, and resources available to focus on the achievement of cultural beauty ideals (Striegel-Moore & Bulik, 2007). Although these factors might influence eating disorder etiology, they are likely not solely responsible for their development (Striegel-Moore & Bulik, 2007). Personality traits such as perfectionism, as well as social anxiety, elevated weight, and high impulsivity, might also play important etiological roles. These sociocultural and environmental factors likely combine with genetic influences (Strober, Freeman, Lampert, Diamond, & Kaye, 2000) to contribute to the development of disordered eating, as is described in the next section.

Behavioral Genetics and Molecular Genetics

The conceptualization of eating disorders has evolved rather radically across time (Vemuri & Steiner, 2007). Previously dominant sociocutural and psychodynamic theories have been supplanted by a biopsychosocial model. This evolution can be attributed in part to a systematic series of family twin and molecular genetics investigations of eating disorders, which have supported the role of familial and genetic factors in liability to eating disorders (Bulik et al., 2006; Klump, Miller, Keel, McGue, & Iacono, 2001). In this section, we review results of family, twin, and molecular genetic studies (for a more thorough review see Trace et al., 2013).

Family studies investigate the degree to which a particular trait runs in families. Although they are a valuable tool, family studies cannot tell us why a trait runs in families—whether due to genetic factors, environmental factors, or some combination of both. The familial nature of AN is well-established. For example, first-degree relatives of patients with AN (parents, children, and siblings) are 11 times more likely to have AN during their lifetime than first-degree relatives of individuals who have never had AN (Strober et al., 2000). Population-based twin studies have provided additional support for the familiality of AN.

Twin studies allow us to examine familial components of disordered eating by comparing similarities and differences in eating problems between monozygotic twins (MZ) and dizygotic twins (DZ). MZ twins are generally assumed to share 100% of their genetic material, whereas DZ twins, on average, share 50% of their genetic material (like brothers and sisters). Variance in liability to a disorder can be dissected into additive genetic factors, shared environmental factors, and unique environmental factors. Additive genetic factors refer to the cumulative effects of many genes, each of which makes a small to moderate contribution. Shared environmental factors reflect environmental influences that affect both members of a twin pair and are believed to make twins more similar. Unique environmental factors (including measurement error), on the other hand, reflect environmental factors that only one twin is exposed to. Unique environmental factors are believed to make twins dissimilar. Twin studies have yielded heritability estimates between 28% and 74% for AN, with the remaining variability largely attributed to unique environmental factors (Klump et al., 2001; Kortegaard et al., 2001; Bulik et al., 2006). Although twin studies can reveal the proportion of individual differences in a disorder that are due to genetic factors, they are unable to identify which specific genes are involved.

Molecular genetic studies provide greater clarity regarding which genes influence risk for a trait or disorder. Association studies examine a genetic variant's association with a trait; if the variant and trait are correlated, there is said to be an association between the two. Association studies that involve a single gene or set of genes that have a hypothesized association with the trait under study are referred to as candidate gene studies. Molecular genetic designs that do not focus on one particular gene or set of genes include linkage and genome-wide association studies (GWAS). Linkage identifies chromosomal regions that house predisposing or protective genes and allow us to narrow the search from the entire human genome to specific regions. GWAS examines 300,000 to 1,000,000 genetic markers scattered across the genome, comparing cases with the trait to controls. If a genetic variant is more frequent in cases, the variant is said to be associated with the trait. GWAS represents an agnostic search of the human genome and as such is a genetic discovery tool.

Decades of candidate gene association studies for AN have examined primarily genes involved in the serotonergic, catecholaminergic, and dopaminergic systems and those affecting appetite and weight regulation. The practice of preselecting a single gene based on presumed biological involvement has fallen out of favor, and it has given way to genome-wide approaches (described next).

Historically, using candidate gene approaches, the serotonergic system received significant attention, and results regarding its importance to eating disorders are inconclusive. One meta-analysis of studies investigating *5-HTTLPR* and AN suggests that carriers of the short allele are at increased risk for this eating disorder (Calati, De Ronchi, Bellini, & Serretti, 2011). A comprehensive review of all candidate gene association studies conducted for AN (175 association studies of 128 polymorphisms related to 43 genes) points to promising although not conclusive evidence for genes related to mood regulation [brain-derived neurotrophic factor *(BDNF)* and *SK3* channel], the hedonic reward system [catecholamine-O-methyltransferase *(COMT)* and opioid receptor-1 *(OPRD1)*], and appetite [agouti-related protein *(AGRP)*] (Rask-Andersen, Olszewski, Levine, & Schiöth, 2010).

Linkage studies identified chromosomes 1, 4, 11, 13, and 15 as possible regions of interest in AN (Bacanu et al., 2005; Devlin et al., 2002; Grice et al., 2002). A follow-up study of candidate genes on chromosome 1 revealed associations with the serotonergic (*5-HTR1D*) and opioidergic (*OPRD1*) neurotransmitter system (Bergen et al., 2003). Genome-wide approaches have been conducted. One Japanese study used deoxyribonucleic acid (DNA) pooling and included only 23K microsatellite markers (Nakabayashi et al., 2009); Wang et al. (2011), conducted GWAS in 1,033 female AN cases and 3,733 pediatric controls; however, no single nucleotide polymorphisms (SNPs), or DNA sequence variation, reached genome-wide significance, which is typical in samples this small. A GWAS conducted under the auspices of the Wellcome Trust Case Control Consortium 3, also underpowered, failed to identify SNPS that reached genome-wide significance (Boraska, in press). Large global efforts are underway to boost sample size in order to identify variants that influence risk for AN (Sullivan, Daly, & O'Donovan, 2012).

Like AN, BN runs in families. First-degree relatives of individuals with BN are 4 to 10 times more likely to have the disorder themselves (Lilenfeld et al., 1998). In studies of female twins, the estimated heritability of BN ranges between 54% and 83% in females (see Slof-Op't Landt et al., 2005, for a review). As is the case in AN, molecular

genetic studies of BN have generally focused on the serotonergic, dopaminergic, catecholamineric, and appetite systems. Significant associations have emerged between BN and *5-HT2A* and *5-HTTLPR*.

Several meta-analyses (Calati et al., 2011; Lee & Lin, 2010; Polsinelli, Levitan, & De Luca, 2012) have examined the association between *5-HTTLPR* polymorphisms and BN, with the large majority suggesting no significant association between *5-HTTLPR* polymorphisms and BN. Investigations exploring associations between other serotonin receptor genes and BN have yielded mixed results (see Scherag, Hebebrand, & Hinney, 2010, for a review). However, associations have been identified between several traits related to BN and the serotonin system, including minimum lifetime BMI (*5-HT1B*), impulsiveness (*5-HT2A* and *5-HTTLPR*), and affective dysregulation in females (*5-HTTLPR*) (see Scherag et al., 2010, for a review). Furthermore, a gene–environment interaction was identified in one study; within a sample of individuals with BN, carriers of the *5-HTTLPR* short allele who reported physical or sexual abuse also manifested greater sensation seeking, insecure attachment, and dissocial behavior (Steiger et al., 2007, 2008). The existence of this type of gene–environment interaction might explain some of the inconsistent results regarding serotonin to date.

Studies investigating genes within the dopamine and catecholamine systems and those genes involved in appetite have also yielded inconsistent findings. Nisoli et al. (2007) examined the prevalence of TaqA1 polymorphisms of the *DRD2* gene in individuals with eating disorders, including BN, and in controls. No significant associations were found between the A1+ allele in BN for either the A1/A1 or A1/A2 genotypes. Sporadic associations were found between BN and the dopamine transporter gene (*DAT1*) (Shinohara et al., 2004) and *COMT* (Mikolajczyk, Grzywacz, & Samochowiec, 2010), respectively. In addition, a few studies have identified an association between BN and preproghrelin (Miyasaka et al., 2006) and *BDNF*, yet these results require replication.

Only one linkage study has been conducted for BN, which examined 308 multiplex families identified through a patient with BN. Significant linkage was found on chromosome 10 and another region on chromosome 14 met criteria for genome-wide-suggestive linkage (Bulik et al., 2003). No GWAS of BN have been conducted to date. In sum, results of molecular genetic studies of BN remain inconclusive and are limited by the use of small samples, which provide relatively low power.

The study of BED has burgeoned in the past decade. However, as the disorder has been more recently operationalized than AN and BN, less research on the genetics of BED has emerged. Nonetheless, extant family, twin, and molecular research largely suggests that familial and genetic factors influence risk for BED. A small number of family studies have been conducted (Fowler & Bulik, 1997; Hudson et al., 2006; Lee et al., 1999). With the exception of the Lee et al. investigation, these studies suggest that BED is familial. This has been further corroborated by twin studies. Two population-based twin studies have examined the heritability of BED (Javaras et al., 2008; Mitchell et al., 2010) and reported heritability estimates ranging from 39% to 45%.

Candidate gene association studies of binge eating and BED have focused on neurotransmitter systems, such as the 5-HT and DA systems, and genetic variants implicated in appetite and obesity. One small case control investigation, comparing women with BED to normal women without BED, was conducted exploring the role of the 5-HTTLPR polymorphism in BED (Monteleone, Tortorella, Castaldo, & Maj, 2006).

The homozygous long-allele and the heterozygous long-allele genotypes were found to be more prevalent in individuals with BED than those without BED. Results may suggest a role of the 5-HTTLPR polymorphism in BED; however, results should be considered preliminary, as the sample sizes in this study were small. Several investigations have also examined the role of DA polymorphisms, and particularly polymorphisms of the DRD2 gene, in BED (Davis et al., 2008; Davis et al., 2009; Davis et al., 2012). Overall, studies exploring the association of between BED and polymorphisms of the DRD2 gene have been inconsistent, likely due to small sample sizes and a lack of statistical power. The largest study to date (Davis et al., 2012) suggests a potential role of the DRD2 polymorphism Taq1A and C958T in BED; however, additional large-sample replication studies are needed.

Genes associated with obesity have also been investigated for their potential role in BED, given the positive correlation between these conditions. *MC4R* (which is associated with obesity) was examined as an early candidate for BED (Branson et al., 2003), although this finding is not consistently replicated across studies (Hebebrand et al., 2004). Positive associations with *5-HTTLPR* and *DAT1, BDNF,* and ghrelin have also been identified in BED (Davis et al., 2007; Monteleone, Tortorella, Castaldo, Di Filippo, & Maj, 2007; Monteleone, Tortorella, et al., 2006; Monteleone, Zanardini, et al., 2006; Shinohara et al., 2004); however, these results require confirmation and replication, and the field awaits more comprehensive genome-wide approaches.

Neuroanatomy and Neurobiology

Neurobiological vulnerabilities contribute to eating disorder pathogenesis (Kaye, 2008; Kaye, Wierenga, Bailer, Simmons & Bischoff-Grethe, 2013; Treasure & Campbell, 1994), and brain structural and functional abnormalities are consistently found in individuals with eating disorders (Frank, Bailer, Henry, Wagner, & Kaye, 2004; Kaye, Fudge, & Paulus, 2009). In addition, numerous behavioral traits associated with AN, including premorbid anxiety, obsessive behaviors, negative emotionality, impaired cognitive flexibility, increased harm avoidance and perfectionism, and altered interoceptive awareness, are hypothesized to be related to underlying abnormalities or alterations in brain structure and function (Kaye et al., 2013). Marsh et al. (2011) reported evidence of deactivation in the inferior frontal gyrus and neural system encompassing the posterior cingulate cortex and superior frontal gyrus in female adolescents with bulimia in comparison to controls during the Simon spatial incompatibility task. This paradigm allowed them to observe abnormal patterns of frontostriatal activation in adolescents with bulimia when engaging in self-regulatory processes associated with conflict resolution. They suggested that this pattern could explain how feeding behaviors might be "released" from regulatory control in conflict situations, thereby perpetuating bulimic behaviors.

Brain structural abnormalities in eating disorders have been investigated using computerized tomography (CT) and magnetic resonance imaging (MRI). Functional imaging studies, including positron emission tomography (PET), single photon emission computer tomography (SPECT), and functional magnetic resonance imaging (fMRI), have also been employed to provide information about the cerebral activity of a system or receptor being studied. Improvements in technology over the last decade,

particularly in neuroimaging and genetics, have greatly enhanced our ability to characterize the complex neuronal systems involved in disordered eating (Kaye, 2008; Kaye et al., 2013). However, these techniques are still relatively new, and our understanding of the relation between biological vulnerabilities and subsequent changes in brain pathways contributing to disordered eating are limited. Neurobiological investigations of disordered eating are further complicated by state-related effects from changes in diet and weight, which impact neuronal processes. Brain imaging is not at a point yet where it can be used diagnostically; however, with the refinement of imaging hardware and improved models of the neurobiology and genetics of psychiatric illness, scientists are hopeful that in the future, imaging will allow us to untangle the complexities of eating disorders, predicting illness development, treatment response, and long-term prognosis (Frank, 2013). At present, central nervous system (CNS) dysregulation of neuropeptides (Bailer & Kaye, 2003) and monoamines (Bailer et al., 2007; Kaye, 2008) as well as brain structural abnormalities (Artmann, Grau, Adelmann, & Schleiffer, 1985; Heinz, Martinez, & Haenggeli, 1977; Joos et al., 2010; Krieg, Lauer, & Pirke, 1989), are implicated in the neurobiology of disordered eating.

Neuropeptides Neuropeptides involve a complicated interplay between the peripheral system and the CNS (Morton, Cummings, Baskin, Barsh, & Schwartz, 2006), and opioid peptides, corticotropin-releasing hormone (CRH), vasopressin, oxytocin, neuropeptide-Y, Peptide YY (PYY), cholecystokinin (CCK), leptin, ghrelin, and gastrin-releasing peptides are reported to play an important role in the regulation of feeding behavior (Bailer & Kaye, 2003; Monteleone, 2011; Yagi et al., 2012). A growing body of literature documents alterations in neuropeptides in individuals with eating disorders (for a recent in-depth review see Monteleone & Maj, 2013). Briefly, individuals with AN have state-dependent altered levels of CRH (Licinio, Wong, & Gold, 1996), neuropeptide-Y (NPY), beta-endorphin, and leptin that normalize with weight restoration (Bailer & Kaye, 2003; Kaye, 2008), whereas individuals with BN demonstrate state-related reductions in cholecystokinin (CCK) response (Brewerton, Lydiard, Laraia, Shook, & Ballenger, 1992; Hannon-Engel, 2012; Kaye et al., 1987; Lesem, Berrettini, Kaye, & Jimerson, 1991) and beta-endorphin levels.

A number of the CNS neuropeptides implicated in AN and BN are also involved in regulating cognitive functioning, mood, the autonomic nervous system, and hormone secretion (Jimerson & Wolfe, 2006). While abnormalities in neuropeptide systems typically remit following recovery from AN and BN, malnutrition in combination with neuropeptide alterations can exaggerate symptoms of increased satiety and dysphoric mood, which might perpetuate eating disordered behavior (Bailer & Kaye, 2003; Monteleone & Maj, 2013); see Bailer and Kaye and Monteleone and Maj for full reviews of how neuropeptides influence AN and BN.

Neuropeptides are also implicated in BED, and both human and animal studies suggest that binge eating alters the endogenous opioid system (Bencherif et al., 2005; Blasio, Steardo, Sabino, & Cottone, in press; Munsch, Biedert, Meyer, Herpertz, & Beglinger, 2009). Individuals with BED have higher meal-induced levels of CCK and PYY than controls (Munsch et al., 2009). Furthermore, both obese and nonobese women with binge eating demonstrate decreased levels of ghrelin in the morning, compared with nonobese healthy women and obese non-binge-eating women

(Monteleone et al., 2005). However, these findings have not been consistently replicated across studies (Geliebter, Hashim, & Gluck, 2008; Munsch et al., 2009).

Monoamines The monoamine system, including serotonin (5-HT), dopamine (DA), and norepinephrine (NE), has also been implicated in the development and maintenance of disordered eating (Hildebrandt, Alfano, Tricamo, & Pfaff, 2010; Kaye et al., 2009; Steiger, 2004; Vaz-Leal, Rodriguez-Santos, Garcia-Herráiz, & Ramos-Feuntes, 2011). The 5-HT system is critical in regulating appetite, anxiety, and impulse control (Fairbanks, Melega, Jorgensen, Kaplan, & McGuire, 2001), and the effects of 5-HT manipulation on eating behaviors have been demonstrated in both animal and human models (e.g., Blundell, 1986; Mancilla-Diaz, Escartin-Perez, Lopez-Alonso, & Cruz-Morales, 2002).

Studies of individuals with eating disorders document alterations in 5-HT metabolism, receptor sensitivity, and transporter activity (Bailer et al., 2011; Frank & Kaye, 2005; Kaye, 2008). As a general trend, decreased 5-HT is associated with increased feeding (Brewerton, 1995), leading to the expectancy that AN would coincide with increased 5-HT.

At first glance, individuals with AN appear to contradict expectation with regard to levels of 5-HT. Individuals with AN have significant reductions in cerebral spinal fluid 5-hydroxyindoleacetic acid (CSF 5-HIAA) compared with controls (Kaye et al., 2009), suggesting reduced 5-HT activity. However, CSF 5-HIAA levels are elevated following long-term recovery from AN (Kaye, 2008), indicating that AN may correspond to a primary state of increased 5-HT and that diminished 5-HT activity may be a result of malnutrition, rather than a trait-related feature.

PET and SPECT have been used to investigate the role of the 5-HT_{1A} and 5-HT_{2A} receptors in AN (Bailer & Kaye, 2011). Although studies have not been entirely consistent, most have shown that both ill and weight restored individuals with AN have reduced binding of 5-HT_{2A} (Bailer et al., 2004; Frank et al., 2002; Kaye et al., 2001) and increased binding of 5-HT_{1A} (Bailer et al., 2005; Bailer et al., 2011). In an animal model, interactions between 5-HT_{1A} and 5-HT_{2A} in the medial prefrontal cortex have been implicated in anxiety, attention, impulsivity, and compulsive behavior (Carli, Baviera, Invernizzi, & Balducci, 2006; Krebs-Thompson & Geyer, 1998; Winstanley et al., 2003). This is an interesting finding given that these traits have been implicated in AN, and particularly AN binge-purge type (AN-BP).

Findings in acute BN are generally compatible with a low 5-HT hypothesis (decreased 5-HT promotes increased feeding). Individuals with BN demonstrate decreased CSF 5-HIAA levels (Kaye, 2008) that are inversely related to binging and purging frequency (Jimerson, Lesem, Kaye, & Brewerton, 1992), reduced platelet binding of 5-HT uptake inhibitors, reduced availability of central transporters, and decreased neuroendocrine responses to 5-HT precursors and 5-HT agonists/partial agonists. However, similar to individuals with AN, following recovery, they have elevated levels of CSF 5-HIAA compared to controls (Kaye, 2008). Abnormalities in 5-HT have also been implicated in binge eating (Akkermann, Nordquist, Oreland, & Harro, 2010) and in the frequency of binge eating for individuals with BN (Jimerson et al., 1992; Monteleone, Brambilla, Bortolotti, Ferraro, & Maj, 1998). Decreased 5-HT responses are hypothesized to contribute to blunted satiety, which may increase propensity for binge eating (Chiodo & Latimer, 1986).

Further support of the role of 5-HT in eating disorders is provided by studies indicating that selective serotonin reuptake inhibitors (SSRIs) are fairly efficacious in treating BN and BED (see Brownley, Berkman, Sedway, Lohr, & Bulik, 2007; Shapiro et al., 2007 for reviews). Fluoxetine is the only FDA-approved medication for the treatment of any eating disorder. Fewer investigations have examined the effectiveness of SSRIs in treating AN, and in the small number of available studies (Attia, Haiman, Walsh, & Flater, 1998; Ferguson, La Via, Crossan, & Kaye, 1999; Kaye et al., 2001; Rosenblum & Forman, 2003; Vaswani, Linda, & Ramesh, 2003; Walsh et al., 2006), results were mixed.

In summary, significant evidence suggests an overall dysregulation of 5-HT in eating disorders (Steiger, 2004; Kaye et al., 2013), which persists following recovery. Together, these results suggest that patterns of 5-HT dysregulation might vary by eating disorder subtype, suggesting that underlying pathophysiology might differ across varying eating disorders presentations (Bailer et al., 2013; Kaye, 2008).

Dopamine is another monoamine hypothesized to contribute to disordered eating (Bailer et al., 2013; Bello & Hajnal, 2010; Frank & Kaye, 2005; Jimerson et al., 1992; Kaye, Frank, & McConaha, 1999), and it is known to be involved in the reward and motivational aspects of feeding behavior (Erlanson-Albertsson, 2005; Szczypka, Rainey, & Palmiter, 2000). Individuals in recovery from restricting-type AN (AN-R) show lower CSF levels of the DA metabolite homovanillic acid (HVA; Kaye et al., 1999), which is typically considered an indicator of reduced dopamine function and reduced dopamine turnover (dopamine to HVA ratio). Individuals recovered from AN-R and AN-BP also demonstrate increased binding of D2/D3 receptors in the anteroventral striatum (AVS; Bailer et al., 2013; Frank et al., 2005), including the nucleus accumbens, a brain region implicated in the response to reward stimuli (Delgado, Nystrom, Fissell, Noll, & Fiez, 2000; Montague, Hyman, & Cohen, 2004).

Individuals with BN, particularly those with high binge frequency, also have significantly lower HVA levels (Jimerson et al., 1992; Kaplan, Garfinkel, Warsh, & Brown, 1989; Kaye et al., 1990). However, Jimerson et al. (1992) found that after weight restoration and normalization of food intake, individuals recovered from BN did not differ significantly from controls on HVA concentrations, suggesting that abnormalities in the dopamine system in BN might be state dependent. Lastly, DA has also been hypothesized to play a role in binge eating disorder by modulating reward pathways (Bello & Hajnal, 2010; Mathes, Brownley, Mo, & Bulik, 2009).

Norepinephrine (NE) transmission in the medial prefrontal cortex is also implicated in food-related motivational behavior in animal models (Ventura, Latagliata, Morrone, La Mela, & Puglisi-Allegra, 2008; Ventura, Morrone, & Puglisi-Allegra, 2007). Although few investigations have specifically examined the role of NE in disordered eating, it plays a central role in CNS modulation of energy balance, which has downstream effects on satiety, hunger, and feeding behavior (Hainer, Kabrnova, Aldhoon, Kunesova, & Wagenknecht, 2006).

Overall, the field is embracing more complex systems and pathway-driven models of disease to understand the complicated way in which monoamines and other neurotransmitters are implicated in disease etiology (Kaye, 2008; Kaye et al., 2009). Further, there is evidence to suggest that these neurotransmitter systems likely act in concert, contributing to behaviors associated with disordered eating. For example, a

recent study by Bailer et al. (2013) using PET showed that an interaction between the 5-HT transporter and striatal DA D2/D3 receptor radioligand binding measures was associated with harm avoidant symptoms in women recovered from eating disorders. Based on this finding, authors hypothesize that interactions between the 5-HT and DA systems may contribute to eating disorder symptoms.

Structural Abnormalities Neuroimaging studies with CT show neuroanatomical changes in individuals with AN, including cerebral atrophy and enlarged ventricles (Artmann et al., 1985; Heinz et al., 1977; Krieg et al., 1989; Lankenau, Swigar, Bhimani, Luchins, & Quinlan, 1985; Nussbaum, Shenker, Marc, & Klein, 1980; Titova, Hjorth, Schiöth, & Brooks, 2013). A 2012 systematic review by Van den Eynde et al. reported that the eight studies they included found reduced gray matter volume in AN in the insula, frontal operculum, and occipital, medial temporal, or cingulate cortex. MRI studies in AN also demonstrate increased volumes of CSF in association with deficits in both total gray matter and total white matter volumes (Castro-Fornieles et al., 2010; Joos et al., 2010; Katzman et al., 1996; Titova et al., 2013) and enlarged ventricles (Golden et al., 1996). There is much debate over whether these changes persist after successful treatment and weight restoration. Several investigations have reported that neuroanatomical changes persist following normalization of weight (Artmann et al., 1985; Krieg et al., 1989), whereas other studies have found that brain tissue may increase with weight restoration in AN (Roberto et al., 2011) and that structural brain abnormalities are reversible after long-term recovery (Golden et al., 1996; Wagner et al., 2005) but not short-term recovery (Friedrich et al., 2012). Although definitive conclusions cannot be drawn, if lasting brain abnormalities in AN do occur, they might represent residual damage to the brain or persistent abnormal metabolism (Husain et al., 1992). They could also represent underdeveloped areas that originally contributed to the eating pathology (Artmann et al., 1985).

Findings regarding structural abnormalities are mixed (Frank, 2013). Several studies support structural changes in BN, including cerebral atrophy and decreased ventricle size (Hoffman et al., 1989; Krieg et al., 1989). Other studies suggest normal or increased localized gray matter in the orbitofrontal cortex and striatum (Joos et al., 2010). A 2010 study by Schäfer, Vaitl, & Schienle, found that individuals with BN had greater medial orbitofrontal cortex volume relative to controls. Further, in individuals with BN who had increased ventral striatum volumes, purging severity and BMI were correlated with striatal gray matter volume, suggesting a potential correlation between behavioral and neuroanatomical findings. Reductions in inferior frontal regions correlated inversely with symptom severity, age, and Stroop interference scores in the BN group. Marsh et al. (in press) reported significant reductions, in 34 adolescent and adult patients with BN relative to healthy controls, of local volumes on the brain surface in frontal and temporoparietal areas in the BN participants. The authors suggested that this difference could be related to deficits in self-regulation seen in BN. Other studies, however, have found no evidence for neuroanatomical abnormalities in BN (Husain et al., 1992; Joos et al., 2010). Taken together, results from these studies indicate that neuroanatomical abnormalities often occur in individuals with eating disorder, particularly AN. Additional prospective studies are needed to understand whether these abnormalities are a cause or an effect of the disordered eating behavior.

Learning, Modeling, and Life Events

As noted previously, biology only accounts for part of the liability to developing an eating disorder. It is hypothesized that environment, via channels such as learning, modeling, and life events, can contribute to eating disorders risk either directly or indirectly through their influence on genetic expression.

Life Events Stressful life events have long been hypothesized to play an important role in eating disorder etiology (Klump, Wonderlich, Lehoux, Lilenfeld, & Bulik, 2002; Pike et al., 2006; Schmidt, Troop, & Treasure, 1999). However, research in this area is fraught with methodological challenges. Many studies have included exclusively clinical samples of individuals with eating disorder symptomatology, did not include controls, and assessed life events retrospectively (Berge, Loth, Hanson, Croll-Lampert, & Neumark-Sztainer, 2011; Raffi, Rondini, Grandi, & Fava, 2000; Schmidt et al., 1999).

Nonetheless, one investigation that did include a community-recruited sample of women with BN and matched controls suggested that individuals with BN were more likely than controls to experience certain stressful life events (e.g., a major move, illness, pregnancy, physical abuse, and sexual abuse) during the year prior to the beginning of their illness (Welch, Doll, & Fairburn, 1997). There was no association between BN status and the occurrence of other life events (e.g., bereavement, illness of a close relative, friend, or partner, and beginning or ending a romantic relationship) in the last year. In addition, 29% of women with BN experienced none of the life events assessed in the 12 months prior to the onset of their diagnosis.

Adverse life events were also associated with BED risk (in the year prior to the onset of the disorder; Pike et al., 2006), in a study comparing women with BED with psychiatric and nonclinical controls. Specifically, individuals with BED were most likely to report significant changes in life circumstances and relationships during the previous year. Furthermore, compared with the nonclinical controls, women with BED more commonly reported specific adverse events, including physical abuse, perceived risk of physical abuse, safety concerns, stress, and experiences of weight- and shape-related criticism. A major limitation of both the Welch et al. (1997) and Pike et al. (2006) studies as well as many others (e.g., Berge et al., 2011; Mitchell, Mazzeo, Schlesinger, Brewerton, & Smith, 2012; Raffi et al., 2000; Reyes-Rodriguez et al., 2011; Schmidt et al., 1999) is that they relied on participants' retrospective recall of stressful life events, and thus, are vulnerable to memory biases.

A small number of studies of community samples have used a longitudinal approach to investigate the potential role of stressful life events in the onset of disordered eating. For example, Loth and colleagues (Loth et al., 2008) evaluated these constructs in a sample of adolescents and emerging adults enrolled in Project EAT. Respondents reported whether they had experienced a broad range of stressful events within the year prior to assessment. Participants also reported their engagement in "extreme weight control behaviors" (defined as laxative diuretic or diet pill use, and vomiting), and binge eating (assessed via a single item) at both Time 1 (approximately 5 years earlier) and Time 2 (when the sample had a mean age of 20.4). This study is relatively unique in its inclusion of men and women. The most common stressful life event among men was "excessive credit card debt" (reported by 17.8% of

men and 19.3% of women). Among women, the most commonly reported stressor was "termination of a long personal relationship" (reported by 22.9% of women and 17.2% of men). For both men and women, the number of stressful life events was positively associated with binge eating and extreme weight control behaviors. This study adds to the literature because of its longitudinal approach, use of a community sample, and inclusion of men and women. It also assessed stressors not often evaluated in other studies (and not typically considered traumas), such as financial concerns.

The relative influence of both major and minor (i.e., daily) life stressors on eating disorder symptomatology was also evaluated in a recent study of college students (Woods, Racine, & Klump, 2010). Major stressors were assessed for the 12 months prior to the study. Results suggested that daily stress moderated the link between restraint and binge eating, but only in the context of high levels of major life stress. Interestingly, the link between restraint and binge eating was not significant under conditions of high major life stress and low daily stress. The authors concluded that the cumulative effects of both major and daily stressors might overwhelm individuals' coping resources, and lead to eating disturbances, consistent with many prominent theories of eating disorder etiology (e.g., Heatherton & Baumeister, 1991). This study's cross-sectional design is a limitation; however, it does highlight the importance of considering daily stressors when evaluating life events and coping resources, and suggests this is an important construct to consider in future clinical and research efforts.

Smyth and colleagues (Smyth et al., 2008) investigated the influence of traumatic events on young adults' eating disorder symptomatology during their transition to college. Participants reported not only whether they had *experienced* each trauma in their lifetime, but also *its perceived severity* (rated on a 5-point scale). Thus, this study incorporated cognitive appraisal of stressors, an important construct discussed further in the following section. Traumas were assessed at Time 1 only. Trauma severity was positively associated with increases in both restrictive eating and binge eating symptomatology over the course of the first semester of college. There were some differences in the specific types of traumas associated with binge and restrictive eating, respectively. For example, nonpersonal traumas were the only specific trauma type associated with increases in restrictive eating. In contrast, several trauma types (e.g., death of a loved one, parents' separation/divorce) were associated with increases in binge eating over the first semester. A study by Bodell and colleagues (Bodell, Smith, Holm-Denoma, Gordon, & Joiner, 2011) also found that the number of life stressors college students experienced between the fall and spring semesters was associated with some eating disorder symptoms (as measured by the EDI-Bulimia subscale) but not others (restrictive eating, as measured by the EDI-Drive for thinness subscale). This study also assessed a range of stressors, including some especially relevant to college students, such as academic performance.

These findings suggest that some stressful life events might increase susceptibility to some eating disorder symptomatology, but this risk is not uniform and is likely mediated by cognitive processes, such as appraisal distress tolerance, and general coping ability, which are discussed in the following section.

Distress Tolerance Perhaps one reason for the somewhat inconsistent findings regarding the impact of stressful life events on eating disorder symptomatology

is that the impact of these experiences is influenced by the way in which they are appraised and how well individuals cope in response to them. Numerous studies have documented the link between cognitive appraisal and psychological outcomes (Folkman, Lazarus, Dunkel-Schetter, DeLongis, & Gruen, 1986; Folkman, Lazarus, Gruen, & DeLongis, 1986). More recently, the construct of distress tolerance has received attention in the area of eating disorders. This construct seems especially relevant to individuals with eating disorders, as emotion regulation difficulties have long been identified in affected individuals and across eating disorder subtypes (Brockmeyer et al., 2012; deZwaan, Biener, Bach, Wiesnagrotzki, & Stacher, 1996; Harrison, Sullivan, Tchanturia, & Treasure, 2009; Heatherton & Baumeister, 1991), and research has linked poor distress tolerance and eating disorder symptomatology (Anestis, Selby, Fink, & Joiner, 2007). There is also significant comorbidity between eating disorders and posttraumatic stress disorder (PTSD; Mitchell et al., 2012; Reyes-Rodriguez et al., 2011).

Accumulating evidence suggests that dialectical behavioral therapy (DBT; Linehan, 1993), a treatment approach focused on strengthening distress tolerance and emotional regulation skills, is generally effective in reducing eating disorder symptomatology (see Bankoff, Karpel, Forbes, & Pantalone, 2012). However, as noted by Bankoff and colleagues, more research is needed to compare DBT with other empirically supported treatments for eating disorders. In addition, these investigations should also directly assess affect regulation, a construct fundamental to the theoretical framework underlying DBT.

Gene-environment interactions also likely play an important role in the relations among adverse events, coping, and eating disorder outcomes. In one of the few studies in this area, Akkerman and colleagues (Akkerman et al., 2012) investigated the role of the 5-HTTLPR genotype and environmental stressors on eating disorder symptoms. The short (*s*) allele of the 5-HTT polymorphic region is positively associated with several mental health outcomes, including neuroticism (Sen et al., 2004). Akkerman and colleagues' sample included girls from the longitudinal Estonian Children Personality, Behaviour and Health Study. Two assessment points were used in the analyses (Time 1 *Mean* age = 14.8; Time 2 *Mean* age = 17.8). Participants reported the lifetime occurrence of specific life events at Time 1; eating disorder symptoms (EDI-Bulimia and EDI-Drive for Thinness) were assessed at Time 2. Results indicated that the 5-HTTLPR genotype was not significantly associated with eating disorder symptomatology; however, this polymorphism interacted with life events to predict higher scores on the EDI-Bulimia subscale at Time 2. Individuals with both this genotype and more negative life events by age 15 were more likely than their peers to report bulimic symptoms at age 18. There was no significant main or interaction effect between genotype and Drive for Thinness.

Mixed results were obtained in related study investigating interactions between genetic influences and a specific life stressor, parental divorce, in a sample of female twins (Suisman, Burt, McGue, Iacono, & Klump, 2011). Parental divorce was not associated with most forms of eating disorder symptomatology measured (binge eating, weight preoccupation, and total disordered eating); however, it was associated with body dissatisfaction. A limitation of both the Akkerman et al. (2012) and Suisman et al. (2011) studies is that it is unclear when the stressor(s) occurred in relation to the precise onset of eating disorder symptomatology. Nonetheless, these two studies

extend the prior literature on life events, eating disorders, and the stress response, and highlight the complexity of these relations.

Cognitive Functioning

The possibility that there is CNS dysfunction in affected individuals has been explored through a variety of mechanisms including neuropsychological performance (Duchesne et al., 2004; Jáuregui-Lobera, 2013). Cognitive functions implicated in AN include decreased attentional capability (Ferraro, Wonderlich, & Jocic, 1997; Giel et al., 2011; Green, Elliman, Wakeling, & Rogers, 1996; Jones, Duncan, Brouwers, & Mirsky, 1991), memory (Kingston, Szmukler, Andrewes, Tress, & Desmond, 1996; Mathias & Kent, 1998), visuo-spatial construction (Thompson & Spana, 1991), learning capacity (Witt, Ryan, & Hsu, 1985), and executive functioning (Kingston et al., 1996; Szmukler et al., 1992). Cognitive functioning in BN has been less extensively studied and has largely focused on decreased attention and executive functioning (McKay, Humphries, Allen, & Clawson, 1986; Steiger, Lehoux, & Gauvin, 1999).

Various deficits in executive functioning have been noted in the eating disorder literature (Cooper, Anastasiades, & Fairburn, 1992; Fassino et al., 2002; Jáuregui-Lobera, 2013; Kemps, Tiggemann, & Marshall, 2005; Koba, Horie, & Nabeta, 2002; Tchanturia et al., 2004; Tchanturia et al., 2012; Zastrow et al., 2009). For example, individuals with AN score lower than controls on executive functioning tasks (Lena, Fiocco, & Leyenaar, 2004). Fassino et al. (2002) and Koba et al. (2002) found that individuals with AN made significantly more errors on the Wisconsin Card Sorting Task (WCST; Berg, 1948), a test of frontal lobe functioning implicated in executive functioning. In addition, Tchanturia et al. (2004) found that individuals with AN performed significantly worse than controls on multiple tests of mental flexibility, another indicator of executive functioning.

Set shifting, or the ability to move back and forth between tasks or mental sets, is an important component of executive functioning (Miyake et al., 2000). Set-shifting ability is essential for cognitive and behavioral flexibility, allowing an individual to adapt his or her behavior to meet the changing demands of the environment. Problems in set shifting might manifest in a variety of forms of cognitive inflexibility (e.g., rigid approaches to problem solving) or response inflexibility (e.g., perseverative or stereotyped behavior; Roberts, Tchanturia, Stahl, Southgate, & Treasure, 2007). Recent research has suggested that set-shifting difficulties might be related to the development of disordered eating (Danner et al., 2012; Kanakam, Raoult, Collier, & Treasure, 2013; Roberts et al., 2007; Steinglass, Walsh, & Stern, 2006; Tchanturia et al., 2004; Zastrow et al., 2009).

For example, individuals with AN perform poorly on set-shifting tasks compared to controls. A 2007 systematic review and meta-analysis (Roberts et al., 2007) examined set shifting in eating disorders. Fifteen papers that administered at least one of six neuropsychological set-shifting tasks—including the Trail Making Test (TMT; Reitan, 1958), the WCST (Berg, 1948), the Brixton Task (Burgess & Shallice, 1997), the Haptic Illusion (Tchanturia, Serpell, Troop, & Treasure, 2001; Uznadze, 1966), the CatBat Task (Eliava, 1964), and the set-shifting subset of the Cambridge Neuropsychological Tests Automated Battery (CANTAB; Downes et al., 1989) to individuals with eating disorders—were reviewed. A consistent deficit was observed

that traversed diagnoses, state of illness, and the majority of the set-shifting assessment measures used. The size of the pooled effect between tasks ranged from small (TMT), to moderate (WCST and CatBat task), to large (Haptic Illusion). Although this study employed a limited amount of data from recovered/weight-restored subgroups of individuals with AN, preliminary results suggest that deficits in set shifting, particularly as measured by the TMT, the Haptic Illusion, and the CatBat, remain following weight restoration (Roberts et al., 2007).

A 2004 study by Tchanturia et al. (2004) examined whether suboptimal set shifting was state or trait related by examining set shifting in individuals with current or past AN. The association of these deficits with obsessive-compulsive behaviors and traits was also explored. The authors compared set-shifting abilities in females with current AN (AN-R, $n = 20$; AN-BP, $n = 14$) prior to receiving treatment, individuals with past AN in long-term recovery ($n = 18$, stable body mass for minimum of a year, regular menses for a year, and no psychotropic medication for a year), and healthy controls ($n = 36$). Participants were given a battery of neuropsychological tests assessing various facets of set shifting and executive functioning. A computerized version of the TMT (Kravariti, Morris, Rabe-Hesketh, Murray, & Frangou, 2003; Reitan, 1958) assessed rapid simple alternation between mental sets; the Brixton Test (Burgess & Shallice, 1997), the Set Flexibility Picture Test (Surguladze, 1995), and the CatBat Task were used to assess problem solving and set shifting. The Uznadze Illusion Task (Uznadze, 1966) was used to assess perceptual set shifting. Lastly, a verbal fluency test (as described in Lezak, 1995) assessed cognitive retrieval and flexibility in cognitive search options. In addition, a semistructured interview evaluated obsessive-compulsive traits in childhood and adulthood.

Scores of individuals with current AN-R or AN-BP on several set-shifting tasks (e.g., including the TMT and the Brixton Illusion) were significantly lower than those of the recovered and control groups. Individuals recovered from AN had significantly more illusions on the Uznadze Illusion Task and made more errors on the Set Flexibility Picture Test, relative to the control group. Overall, the individuals recovered from AN obtained scores that were between those of individuals with current AN and healthy controls, suggesting that nutritional status might play some role but is not entirely responsible for the mental inflexibility associated with AN.

Across studies, findings suggest that executive functioning deficits might be related to an underlying biological vulnerability to AN. Neurobiological deficits found among individuals with AN might mirror the behavioral and personality characteristics, such as rigidity and inflexibility, observed within this diagnostic group (see reviews by Braun & Chouinard, 1992; Jáuregui-Lobera, 2013; Lauer, 2002).

Effortful control may represent one domain that differs clearly between the restricting subtype of anorexia nervosa, in which it is presumed that individuals use high levels of cognitive control, especially in relation to eating (van Elburg & Treasure, 2013), and those with eating disorders characterized by binge eating or purging, which may represent a deficit in top-down control of biological reactivity to reward and emotion (Claes, Mitchell, & Vandereycken, 2012).

Finally, many individuals with anorexia nervosa also appear to have social cognitive deficits (van Elburg & Treasure, 2013; Zucker et al., 2007). Some patients report long-standing interpersonal discomfort even premorbidly, and long-term outcome studies of anorexia nervosa suggest a higher proportion of individuals

with traits characteristic of the autism spectrum (see Zucker et al. for a comprehensive review). Of course, all studies of cognitive function in eating disorders must carefully consider the impact of nutritional state on functioning. Planned and ongoing investigations of high-risk cohorts, unaffected relatives, and long-term recovered individuals have the potential to disambiguate state from trait deficits.

Racial-Ethnic Considerations

African American women's risk for AN and BN is generally found to be lower than that of White women (Hoek, 2006; Striegel-Moore et al., 2003); thus, for many years, eating disorders were often considered illnesses that affected White women nearly exclusively (Becker, Franko, Speck, & Herzog, 2003). This cultural stereotype appears to have influenced clinicians as well, as studies show that women of color are less likely to be identified as having an eating disorder (even when their symptoms are consistent with diagnosis) or referred for eating disorder treatment (Becker et al., 2003).

As noted previously, lifetime prevalence estimates of *DSM-IV* AN, BN, and BED from a nationally representative population sample of women over age 18 are 0.9%, 1.5%, and 3.5% (Hudson et al., 2007). Prevalence estimates vary across racial and ethnic groups, however. The lifetime prevalence of eating disorders among African American adult females from a U.S. population-based survey is 0.14% for AN, 1.90% for BN, 2.36% for BED, and 5.82% for any binge-eating behavior (Taylor, Caldwell, Baser, Faison, & Jackson, 2007). Other studies have reported slightly lower prevalence estimates in African American women (Striegel-Moore et al., 2003). One set of lifetime prevalence estimates among Latinas are 0.12% for AN, 1.91% for BN, 2.31% for BED, and 5.80% for any binge eating (Alegria et al., 2007). Relatively similar estimates were obtained in a more recent population-based sample (Marques et al., 2011).

The prevalence of eating disorders among Asian women has been estimated to be 0.12% for AN, 1.42% for BN, 2.67% for BED, and 4.71% for any binge eating (Nicdao, Hong, & Takeuchi, 2007). These numbers are subject to interpretation, as another study found no difference in binge-eating frequency by race (Reagan & Hersch, 2005).

African American women's risk for binge eating and BED may indeed be equal to, or possibly even greater than, that of White women (Striegel-Moore, Wilfley et al., 2000). For example, Taylor et al. (2007) found that BED was not only more common than either AN or BN among African American women, but also was the most chronic eating disorder diagnosis, with a mean duration of over 7 years. These findings are consistent with those of other studies with respect to the clinical significance and prevalence of binge-eating behaviors among African American adults (Marcus et al., 2007; Striegel-Moore, Wilfley et al., 2000). Another significant concern regarding eating disorders among African Americans is that rates of treatment seeking for eating disorders are significantly lower among this group than among White women (Becker et al., 2003; Cachelin, Veisel, Barzengarnazari, & Striegel-Moore, 2000; Marques et al., 2011). These findings suggest that many African American women with clinically significant binge-eating behaviors remain untreated.

The few extant studies on eating disorders in Latinos suggest prevalence estimates on par with Whites in the United States (Alegria et al., 2007; Reyes-Rodriguez et al., 2010). One recent study found that Latinas were more likely than White women to

report lifetime BN compared with White women (Marques et al., 2011). Studies of eating disordered attitudes and behaviors indicate considerable concern among Latinas. Pumariega (1986) found that 20% of young Hispanic urban high school students scored 30 or higher, the screening threshold, on the Eating Attitudes Test (EAT). Binge eating has also been reported to be more severe in Latinas than in Whites or African Americans (Fitzgibbon et al., 1998). Latina girls report greater body dissatisfaction than White girls (Robinson et al., 1996) and more disturbed eating attitudes and behaviors than African American girls (Vander Wal & Thomas, 2004). Weight-related concerns and behaviors are prevalent among adolescents, regardless of their ethnic or racial origin (Neumark-Sztainer et al., 2002).

Although research is emerging regarding the prevalence of eating disorders across racial and ethnic groups, much less is known about the treatment of eating disorders in diverse populations. The majority of studies constituting the evidence base have been conducted primarily on White samples. This is especially concerning, as results of one recent study indicated that African Americans were more likely than Whites to drop out of treatment for BED (Thompson-Brenner et al., 2013). Research testing the appropriateness of standard eating disorders treatments and the optimal approaches to cultural adaptation of treatments for diverse populations remains in its infancy.

COURSE AND PROGNOSIS

AN has serious medical and psychological consequences, many of which persist even after recovery. In addition to the eating-related symptomatology, many other comorbidities of this disorder, including depression, anxiety, social withdrawal, heightened self-consciousness, fatigue, and multiple medical complications, cause considerable impairment (Berkman, Lohr, & Bulik, 2007). For example, the social toll of AN interferes with normal adolescent development (Bulik, 2002). Across psychiatric disorders, the highest risks of premature death, from both natural and unnatural causes, are from substance abuse and eating disorders (Harris & Barraclough, 1998).

AN history is further associated with reproductive problems (Bulik et al., 1999; Micali, Simonoff, & Treasure, 2007; Micali & Treasure, 2009), osteoporosis (Mehler & MacKenzie, 2009), continued low BMI (Sullivan, Bulik, Fear et al., 1998), and major depression (Fernandez-Aranda et al., 2007). Given the high morbidity and mortality associated with AN, it is critical to develop effective treatments. Initial treatment typically includes a comprehensive medical evaluation and nutritional counseling. Less medically compromised cases of AN are most often treated on an outpatient basis by mental health providers, with primary-care physicians managing medical issues. Treatment guidelines or position papers outlining recommended AN treatment have been developed by numerous professional organizations, including the American Psychiatric Association (APA, 2006), the National Institute for Clinical Excellence (NICE, 2004), the Society for Adolescent Medicine (Golden et al., 2003), the American Academy of Pediatrics (AAP, 2003), and the Royal Australian and New Zealand College of Psychiatrists (Beumont et al., 2004).

AN treatment also typically involves psychotherapeutic intervention. Individual, family, and group psychotherapy for AN are conducted from a multitude of theoretical perspectives (e.g., cognitive-behavioral, interpersonal, behavioral, and psychodynamic). For children, family-based therapy has received considerable attention, and

it is generally suggested that family members be included in treatment, when feasible and sensible. The current evidence base for treatment of AN suggests some benefit for family-based treatment for youth and recommends a combination of renourishment and psychotherapy (specialist supportive clinical management, CBT, or IPT) for adults (Watson & Bulik, 2013). Adults with AN have typically been treated entirely on an individual basis, often leaving partners unsure about how best to assist. A new intervention currently being studied, Uniting Couples (in the treatment of) Anorexia Nervosa (UCAN), leverages the power of interpersonal relationships by incorporating the partner into treatment using a cognitive-behavioral couple therapy approach. UCAN explores several domains (core AN symptoms, body image, affection, sexuality, relapse, and recovery) and helps partners learn to provide support for the patient and reinforce appropriate eating and healthy behaviors, while also improving general relationship functioning (Bulik, Baucom, Kirby, & Pisetsky, 2011).

The APA Working Group on Eating Disorders recommends hospitalization for individuals below 75% of ideal body weight (APA, 2006). However, in addition to weight, parameters such as medical complications, suicidality, previous treatment success, psychiatric comorbidities, social support, role impairment, and availability of other treatment options should all be considered in level-of-care decisions (APA, 2006). Currently, no medications are effective in the treatment of AN (Bulik, Berkman, Brownley, Sedway, & Lohr, 2007). Although commonly prescribed, SSRIs tend to be ineffective in the underweight state, especially in the absence of dietary tryptophan to subsidize the synthesis of serotonin. All treatment commonly involves highly specialized multidisciplinary teams, including psychologists, psychiatrists, internists or pediatricians, dietitians, social workers, and nurse specialists.

Among individuals hospitalized for AN, lengths of stay are much shorter in the United States, compared with those in Europe and New Zealand. For example, Striegel-Moore et al. found the average length of stay within the United States was 26 days (according to an insurance database of approximately 4 million individuals) (Striegel-Moore, Leslie, Petrill, Garvin, & Rosenheck, 2000). This is substantially shorter than stays found in other countries, including New Zealand (72 days; McKenzie & Joyce, 1992) and Europe, which ranges from 40.6 days (Finland) to 135.8 days (Switzerland) (Matthias, 2005). Moreover, AN treatment costs in the United States were higher than those for obsessive-compulsive disorder and comparable to those for schizophrenia, both of which occur at similar rates to AN (Striegel-Moore, Leslie, et al., 2000).

Patients with BN report physical symptoms such as fatigue, lethargy, bloating, and gastrointestinal problems. Frequent vomiting is associated with electrolyte abnormalities, metabolic alkalosis, erosion of dental enamel, swelling of the parotid glands, and scars and calluses on the backs of their hands (Mitchell & Crow, 2006). Laxative misuse often causes edema, fluid loss and subsequent dehydration, electrolyte abnormalities, metabolic acidosis, and potentially permanent loss of normal bowel function (Mitchell & Crow, 2006).

In the United States, most BN treatment is conducted on an outpatient basis. A comprehensive medical evaluation is typically recommended, given the frequency of medical and nutritional complications within this patient population. If significant medical complications related to BN are present, or if the affected individual is pregnant or unable to bring her or his binge-purge behaviors under control in outpatient treatment, partial hospitalization or inpatient treatment may be warranted.

Once medical issues are assessed and under control, psychotherapy (individual and/or group) is typically the primary treatment for BN. As is the case with AN, the theoretical perspectives used in these psychotherapeutic interventions can vary; however, cognitive-behavioral and interpersonal psychotherapy are commonly used. In 1996, the Food and Drug Administration (FDA) approved fluoxetine for the treatment of BN. Currently, this is the only FDA-approved medication for the treatment of any eating disorder.

Given that BED has only recently entered the psychiatric nomenclature, minimal population-based data are available regarding the morbidity and mortality related to this diagnosis. However, most adults with BED are obese and, thus, are at risk for medical complications associated with overweight (Hudson et al., 2007; Hudson et al., 2010; Striegel-Moore et al., 2001). Global community surveys suggest that the majority of individuals with a lifetime BED diagnosis (79.0%) also meet diagnostic criteria for at least one additional psychiatric disorder (including mood, anxiety, behavioral, and substance use disorders). BED also predicts subsequent onset of arthritis, chronic back/neck pain, chronic headaches, diabetes, hypertension, and ulcers (Kessler, Berglund, et al., 2013). Many adults with BED report that their symptoms began in childhood (Abbott et al., 1998). Thus, it seems important that future research investigate further the correlates of binge eating in childhood. Within the United States, BED treatment is typically conducted on an outpatient basis. Psychological and nutritional interventions aim to reduce binge eating and control weight (Brownley et al., 2007). Common psychotherapeutic approaches include cognitive-behavioral and interpersonal psychotherapy; nutritional approaches include behavioral self-management strategies and facilitating hunger and satiety awareness (Brownley et al., 2007). Pharmacotherapy that targets both the core symptom of binge eating and weight loss (when appropriate) are also available as off-label interventions (Brownley et al., 2007; Peat, Brownley, Berkman, & Bulik, 2012).

CASE STUDY

Referral

Wendy was a 35-year-old married White female who was referred for treatment for an eating disorder after passing out at the finish line of a half marathon.

Presenting Complaints

The emergency room discharge note indicated that Wendy was 5 feet 6 inches tall and 95 pounds (BMI 16.3 kg/m^2). She was severely dehydrated, her potassium was 2.5 (normal range 3.5–5 mEq/L), and her EKG indicated a prolonged QT interval. Pulse and blood pressure were low. The physician noted scrapes on her knuckles (Russell's sign) indicative of purging and referred her to the eating disorders team for follow-up.

History

Wendy was a competitive runner with hopes of qualifying for the Olympics. Two years ago, while on a training run on trails, she was attacked by a man who tried to

rape her. She screamed and fought and managed to get away by running out of the forest as fast as she could, but she continued to have flashbacks to this attack every day when she was training on the streets or trails. Prior to the attack, all her attention was on training. She was a healthy eater, focused on performance rather than appearance, and adhered strictly to the recommendations of her trainer and sports dietitian. After the attack, she became increasingly anxious and had difficulty keeping up her training schedule. Her race times were increasing, as was her weight. She lost two races to one of her main competitors, and when she saw a picture of herself coming in second in the paper, she became fixated on her weight. She was up to 125 pounds, which was higher than she had ever been before. She started cutting back on calories, which she found easy to do. Wendy stated, "I was training hard and pushing through pain to get through marathons, so dealing with hunger is a piece of cake in comparison."

One evening she went out for pizza and beer with her husband and some friends. She went to the restroom and was overcome by anxiety about what she had eaten. She decided to vomit and, much to her surprise, she felt less anxious afterward. At that point, she rationalized that this would be a way to keep people off her case about not eating enough; she could eat, but then get rid of it whenever she wanted. Soon the urge to vomit became overwhelming, and it seemed to be the only way she could control her anxiety. She started a few times a week, but she was soon up to 5 to 10 times a day. Her weight continued to drop and her times kept getting worse. Her coach and trainer were worried about her health, but she denied any problems. She started having difficulty concentrating at work, was sleeping poorly, and withdrew almost completely from her family and friends. She also withdrew from her husband. Even though they had been talking about starting a family, she became less and less interested in having sex and started even disliking being touched. She spent hours in the bathroom scrutinizing her body—checking to see if her shape had changed, pinching the skin on her waist to make sure her shape wasn't changing, and weighing herself—sometimes 10 times per day. She became convinced that the only way to start winning again was to get down to 90 pounds. She was restricting her intake to about 800 calories per day, restricting fluids, and vomiting several times per day. Wendy made it through the half marathon on sheer will, but passing out at the finish line was the final event that brought her into treatment.

ASSESSMENT

On clinical interview, Wendy demonstrated significant weight loss below 85% of expected weight for her age and sex. She presented with clear drive for thinness, fear of weight gain, and denial of illness. Her body image was distorted, as she continued to see herself as fat, even though she was 95 pounds and 5 feet 6 inches tall. There were no other medical explanations for her weight loss. She denied objective binge eating (eating unusually large amounts of food and feeling out of control) but endorsed subjective binge eating (feeling out of control when eating regular or small amounts of food). She also admitted to regular purging via self-induced vomiting. She had not menstruated for the previous 6 months. Wendy met the diagnostic criteria for anorexia nervosa, binge-purge subtype.

Clinical interview also indicated that she experienced posttraumatic stress symptoms secondary to the attack while running. She completed three self-report forms—the Eating Disorders Inventory (EDI) and the Beck Depression and Anxiety Inventories (BDI, BAI). Results indicated high scores on drive for thinness, body dissatisfaction, and perfectionism on the EDI. Her BDI scores indicated mild depression and no suicidal ideation, and a BAI score of 38 indicated high anxiety consistent with her clinical interview.

SUMMARY

Our understanding of eating disorders continues to advance. Once thought to be largely disorders of choice and of primarily sociocultural origin, it is now common knowledge that genes and biology play an important role in risk. Further advancements to understanding the eating disorders are likely to come from neurobiological and genetic research, and these discoveries will facilitate our ability to understand why some individuals are more vulnerable to environmental insults than others. Ironically, the thorough study of biology may provide the biggest boost for our understanding of the role of environment as causal in eating disorders. This work may also assist in identifying risk factors, which will fuel prevention efforts.

As work in the eating disorders field is additionally challenged by the new world context of escalating obesity, eating-disorders researchers must partner with obesity researchers both to share findings and to ensure that prevention and treatment efforts in one area do not increase the risk for development of pathology in the other area. For example, obesity prevention efforts cannot inadvertently lead to more disordered eating behavior in attempts to control weight, and eating disorders treatment should not inadvertently increase the risk for the development of obesity. Animal models of component features of eating disorders (e.g., driven physical activity, binge eating) might also shed valuable light on underlying neurobiological mechanisms that initiate and maintain dysregulated behavior. The integration of research findings from cell to population are required to complete the complex picture of these perplexing disorders that stand at the intersection of psyche and soma.

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CHAPTER 14

Sleep-Wake Disorders

CANDICE A. ALFANO and SIMON LAU

INTRODUCTION

Sleep complaints are common in the general population and highly prevalent among individuals seeking mental health services. The most recent edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5;* American Psychiatric Association [APA], 2013) categorizes sleep disorders into 10 disorders or disorder groups, including: (1) insomnia disorder; (2) hypersomnolence disorder; (3) narcolepsy; (4) breathing-related sleep disorders; (5) circadian rhythm sleep-wake disorders; (6) non-rapid eye movement (NREM) sleep arousal disorder; (7) nightmare disorder; (8) rapid eye movement (REM) sleep behavior disorder; (9) restless legs syndrome; and (10) substance/medication-induced sleep disorder. Notably, the Sleep-Wake Disorders section included in *DSM-5* represent a considerably expanded list in contrast to the previous *DSM* edition (*DSM-IV-TR;* American Psychiatric Association [APA], 2000), which included only four broad sleep disorder categories (i.e., primary sleep disorders, sleep disorders related to another mental disorder, sleep disorders related to a general medical condition, and substance-induced sleep disorders). *DSM-5* also pays more attention to co-existing conditions, emphasizing the need for sleep-directed clinical intervention even when a comorbid medical or mental disorder is present. These significant changes should be viewed as a direct result of the abundance of sleep-focused research conducted within the past decade.

Although mental health researchers and practitioners tend to be most familiar with *DSM* classifications, the *International Classification of Sleep Disorders*, second edition (*ICSD-2*; American Academy of Sleep Medicine, 2005) is commonly used within the field of sleep medicine. The *ICSD-2*, which is consistent in style with the *International Classification of Diseases*, 10th edition (*ICD-10;* World Health Organization, 1994), provides characteristics and diagnostic criteria for over 80 sleep disorders organized into eight broad categories. In addition to a greater breadth of conditions, the *ICSD-2* provides information on validated assessments and treatments.

Because the intent of this chapter is to review sleep disorders most relevant to the mental health professional (i.e., sleep syndromes that are most likely to present in clinical practice), we limit our focus to *DSM-5* sleep-wake disorders likely to be encountered by mental health professionals. Insomnia, hypersomnolence, and narcolepsy are

reviewed in the major section titled "Disorders of Inadequate/Excessive Sleep." The second major section, "Parasomnias," provides a review of disorders characterized by undesirable motor, verbal, or experiential phenomena occurring in association with sleep, specific stages of sleep, or sleep-awake transition phases. Non-rapid eye movement (NREM) sleep disorders, nightmare disorder, and rapid eye movement (REM) sleep behavior disorder are considered parasomnias. Within both sections, information aimed at assisting clinicians to correctly differentiate these from other sleep disorders, such as those related to a mental disorder, general medical condition, or substance use, are discussed in both sections.

Since a fundamental disturbance in brain mechanisms that regulate sleep functions is thought to underlie many sleep disorders (e.g., sleep disorders that cannot be exclusively explained on the basis of a coexisting psychiatric disorder or medical condition), we begin with a brief review of the neuroscience of sleep including the use of polysomnography, considered the "gold standard" for assessing objective sleep patterns. We also provide an overview of actigraphy, which is commonly used in the diagnosis of certain sleep disorders such as circadian rhythm sleep-wake disorders.

NEUROSCIENCE OF SLEEP

At a fundamental level, sleep is exemplified by decreased consciousness, decreased responses to external stimuli, and decreased overall motor activity compared to wakefulness. Several brain neuroanatomical structures, genes, and neurotransmitter pathways play a role in sleep; however, no specific neurobiological mechanism(s) have been identified that specifically control the onset, maintenance, or termination of sleep. Electroencephalography (EEG), combined with electrooculography (EOG) and electromyography (EMG), are the basis upon which the two major types of sleep (i.e., rapid eye movement [REM] versus non-REM sleep), sleep staging (non-REM Stages 1–3), and sleep architecture are defined.

POLYSOMNOGRAPHY (PSG)

When electrodes are placed on the head to record surface brain activity, the resultant information is called electroencephalography (EEG). In order to obtain a comprehensive profile of objective sleep, EEG information must be combined with EOG and EMG recordings; these data together are referred to as polysomnography (PSG). EEG brainwaves are defined by amplitude, frequency, and form/shape, all of which are relevant for interpreting stages of sleep. *Amplitude* refers to the magnitude of the brainwave [from its valley-to-peak (measured in microvolts)]. *Frequency* is the number of peak-to-peak brainwaves over time [measured in cycles per second, referred to as Hertz (Hz)]. Brainwave frequencies are described using the Greek alphabet: Beta (12–30 Hz), Alpha (8–12 Hz), Theta (4–7 Hz), and Delta (up to 4 Hz). Electrooculography (EOG) measures the movement of the eye. During REM sleep, the phase most commonly associated with dreaming, the eyes move back and forth rapidly. Electromyography (EMG) measures muscle tone and activity. With the exception of the heart, eye, and respiratory muscles, there is a loss of muscle tone in all other major muscle groups during REM sleep.

Types of Sleep

Sleep is divided into two major types: REM and non-REM sleep. The brainwaves of REM sleep are similar or essentially identical to the brainwaves of wakefulness (i.e., low voltage, high frequency). For this reason, REM sleep is often referred to as "paradoxical" or "active" sleep. During the PSG, REM sleep can be distinguished from wake based on the appearance of low-amplitude, high-frequency brainwaves (taking on a "sawtooth" shape/form) in the presence of muscle atonia and rapid eye movements. Non-REM sleep is basically any sleep state that is not REM sleep. Rechtshaffen and Kales (1968) originally defined four stages (I–IV) of non-REM sleep, reflecting lighter-to-deeper stages of sleep. In 2007, the American Academy of Sleep Medicine established a new nomenclature combining non-REM stages 3 and 4 into a single category (non-REM stage 3), commonly referred to as "slow wave," "deep," or "delta" sleep.

Sleep Stages

Non-REM Stage 1 (N1) occurs during the transition from wakefulness to sleep. *Non-REM Stage 2 (N2),* which predominates in adults, is associated with theta waves and the appearance of highly characteristic sleep spindle and K-complex wave forms. *Non-REM Stage 3/4 (N3)* is the deepest form of sleep. Some patients report dream content during N3 sleep, but such reports are infrequent and reported images are much less vivid as compared to dreams emerging from REM sleep.

Sleep Architecture

Sleep architecture refers to the cyclical pattern in the types (REM and non-REM) and stages of sleep. There is a predictable pattern in the progression of REM and non-REM sleep. In healthy normal adults, approximately 15–20 minutes of sleep is required to achieve N2 sleep and approximately 30–60 minutes to transition from N2 to deep sleep (N3). After a period of deep sleep, there is a transition back toward lighter (N2) sleep followed by a period of REM sleep. This cycle, referred to as the ultradian cycle, repeats itself, with progressively longer REM periods throughout the night. Each ultradian sleep cycle lasts approximately 90–120 minutes, with four to five cycles during an 8-hour night. The average proportion of time a healthy adult spends in each of type and stage of sleep is 25% REM and 75% non-REM sleep [N1 (5%), N2 (45%–55%), N3 (15%–25%)]. Abnormalities in the timing, distribution, and/or proportion of different types and phases of sleep are prevalent in various sleep disorders and psychiatric conditions (e.g., depression).

Multiple Sleep Latency Test (MSLT) The Multiple Sleep Latency Test (MSLT) is a measure of daytime sleepiness, developed by Carskadon and Dement (1997). The test consists of four to five distinct 20-minute sessions, separated by 2-hour intervals, during which the individual is placed in a comfortable, dark sleep environment (i.e., sleep laboratory) and asked to take a nap. The first nap period begins within 3 hours after awakening from the previous night's sleep. The main purpose of this test is to determine sleep latency and, if present, the presence of REM sleep. Sleep latencies

greater than 10 minutes (including an inability to fall asleep) are considered normal in well-rested individuals, whereas people who fall asleep within 5 minutes are judged to be sleep deprived (i.e., suffering from pathological sleepiness). The MSLT is an objective measure of daytime sleep propensity, and the appearance of REM sleep within 20 minutes is suggestive, but not diagnostic, of narcolepsy.

ACTIGRAPHY

Wrist actigraphy is an objective, noninvasive, and relatively cost-effective means of estimating sleep-wake patterns. The small watch-sized device is worn on the nondominant wrist 24 hours a day. Movement data (i.e., activity level sampled at 10-second intervals and summed across 1-minute intervals) is collected and stored over an extended time (up to several weeks) and then used to determine sleep and wake periods. Event markers provide specific information regarding time in bed versus time asleep. Data are then downloaded onto a computer and scored by a computer-generated algorithm reliable in identifying sleep and wake periods. Common variables derived from actigraphy include total sleep time, sleep-onset latency, wake time after sleep onset, and sleep efficiency. In healthy adults, actigraphy-based estimates of sleep correlate well with PSG data, although as sleep becomes more disturbed, actigraphy-based sleep estimates become less reliable (Ancoli-Israel et al., 2003; Kushida et al., 2001). Actigraphy can nonetheless be highly useful in the diagnosis and management of insomnia and circadian-rhythm sleep-wake disorders.

DISORDERS OF INADEQUATE/EXCESSIVE SLEEP

The term *dyssomnias* was formerly used to refer to a broad group of disorders characterized by problems of initiating and/or maintaining sleep or of excessive sleepiness and disturbance in the amount, quality, or timing of sleep. However, this term was eliminated from ICSD-2 in favor of using more specific diagnostic groupings (e.g., ICSD-2 includes Insomnia as its own category and describes 11 different subtypes of the disorder). In the following three sections, we describe specific disorders: insomnia disorder, hypersomnolence disorder, and narcolepsy. The first two are prevalent disorders and highly likely to be encountered by mental health professionals. The last, narcolepsy, is much less prevalent in the general population, but commonly comorbid with affective and other types of psychopathology.

INSOMNIA DISORDER

Insomnia disorder is largely a subjective complaint of one or more of the following: delayed sleep onset, difficulty maintaining sleep, multiple awakenings from sleep, early morning awakenings, or the failure to feel refreshed after sleeping (i.e., non-restorative sleep). *DSM-5* criteria require at least 1 month of insomnia, as well as secondary impairment in daytime functions (e.g., difficulty concentrating, poor work performance). The sleep difficulty must occur at least 3 nights per week and for at least 3 months. Furthermore, there must be adequate opportunity for sleep. Of note, a change from primary insomnia in *DSM-IV* to insomnia disorder in *DSM-5* was

specifically aimed at avoiding primary versus secondary designation when insomnia co-occurs with other psychiatric/medical conditions.

Epidemiology and Other Features Insomnia is the most prevalent of all sleep disorders in the general population. It is also the most common complaint among patients seeking treatment from primary care physicians and mental health professionals. Dissatisfaction with sleep quantity or quality in insomnia disorder may relate to problems falling and/or staying asleep or nonrestorative sleep, and specific symptoms often change across time. Overall, insomnia symptoms are present in approximately 20% of the population and more prevalent in women and older patients. Although it can be an independent condition, insomnia is most commonly observed as a comorbid condition with a medical or psychiatric disorder. Up to 50% of insomnia patients meet criteria for a comorbid mental health diagnosis, most commonly anxiety or depression (Ford & Kamerow, 1989; Ohayon, Caulet, & Lemoine, 1998).

Hypersomnolence Disorder

Hypersomnolence disorder is characterized by excessive sleepiness for a minimum of 1 month (or less if recurrent). Hypersomnolence is clinically demonstrated either by unusually long sleep episodes or by abnormal amounts of sleeping when the person is expected to be alert. There may be daily episodes of daytime sleep. A person with hypersomnolence disorder sleeps at least 7 hours in a single night and often will sleep 10–14 hours during his or her normal sleeping period. The diagnostic criteria require at least three episodes per week for 3 months and the hypersomnolence must result in functional impairment (APA, 2013).

Epidemiology and Other Features Approximately 5%–10% of patients who seek treatment for excessive daytime sleepiness suffer from hypersomnolence disorder. The disorder is estimated to affect 1% of U.S. and European populations. Males and females are affected equally. The term *hypersomnolence* broadly includes symptoms of excessive quantity of sleep, deteriorated quality of wakefulness, and sleep inertia (i.e., a period of impaired performance or reduced vigilance following awakening from a regular sleep episode). In extreme cases, sleep episodes can last up to 20 hours. Sleep inertia may last several minutes to several hours. "Automatic behaviors" (i.e., routine, low-complexity behaviors that are poorly recalled later) are commonly reported. Onset is often progressive with a mean age of onset between 15 and 25 years and symptoms worsening over time. Prolonged nocturnal sleep and difficulty awakening in the morning can significantly impair occupational, academic, and personal functioning.

Narcolepsy

DSM-5 distinguishes narcolepsy from other forms of hypersomnolence. Narcolepsy is characterized by excessive daytime drowsiness, emotion-triggered muscle atonia/weakness (i.e., cataplexy), sleep paralysis, and hypnagogic/hypnopompic hallucinations. Narcolepsy is defined as irresistible attacks of refreshing sleep with either one or both of the following: cataplexy or recurrent intrusions of REM-related phenomena

such as hypnopompic or hypnagogic hallucinations or sleep paralysis. The severity of sleepiness ranges from feelings of drowsiness while engaged in boring tasks (often requiring naps) to pervasive sleepiness and full-blown sleep attacks.

Cataplexy is an interesting phenomenon, with episodes lasting from seconds to minutes. Among individuals with a longstanding disorder, the episodes consist of bilateral muscle tone loss precipitated by laughter or joking (APA, 2013). In children or people with a more recent onset, cataplexy may consist of facial grimacing or jaw-opening or global hypotonia.

Epidemiology and Other Features The prevalence of classic narcolepsy with emotion-triggered cataplexy is approximately 0.02% to 0.05% of the U.S. population, with an equal incidence in men and women. Onset can be abrupt or progressive. Cataplexy, where the atonia/weakness affects the knees, face, neck/head, or muscles of the lower or upper extremities is a pathognomonic of narcolepsy. However, approximately 30% of narcoleptics suffer from excessive daytime sleepiness and sleep-onset REM but putatively have no history of cataplexy. In children and adolescents, cataplexy can be atypical, affecting only discrete muscle groups (e.g., the face). Presence of cataplexy may be a marker of severity and/or low levels of hypocretin. Approximately 20%–60% of narcolepsy patients report sleep paralysis upon falling sleep or awakening. However, sleep paralysis occurs in normal sleepers as well.

It is widely known that narcoleptics have trouble staying awake. Less appreciated is that narcolepsy is also associated with insomnia. Thus, patients with narcolepsy have problems with maintaining *both* sleep and alertness under the appropriate circumstances. Numerous aspects of the narcoleptic patient's life may be impaired by their symptoms including work/career, travel/driving, socialization and interpersonal relationships. Because narcoleptic patients often appear sleepy, nod off, and/or withdraw from social engagements they are sometimes perceived as lazy, shy, or suffering from a mental disorder.

Diagnostic Considerations *DSM-5* criteria for insomnia and hypersomnolence disorders includes co-occurring medical, psychiatric, and/or other sleep disorders as unique specifiers (rather than exclusions for diagnosis as in *DSM-IV*). From a clinical standpoint, there is a need nonetheless to determine whether sleep complaints are solely caused by another underlying condition. This is often difficult to determine with certainty since so many disease entities can negatively impact sleep. Within this context, generalized anxiety disorder (GAD) is commonly associated with problems initiating, maintaining, or achieving restful sleep. Insomnia is present in up to 70% of patients with GAD (Alfano & Mellman, 2010; Monti & Monti, 2000) and the quality of insomnia in GAD is nearly identical to that of patients with insomnia disorder. In both insomnia and GAD, patients often worry about obtaining sufficient sleep at night and report difficulty falling asleep and maintaining sleep. Both insomniac and GAD patients report being keyed up (alternating with fatigue) and having difficulty concentrating.

Hypersomnolence is common in depressed patients and associations between depression and hypersomnia are likely to be bidirectional. The presence of hypersomnia in major depressive disorder (MDD) has been hypothesized to reflect abnormal sleep homeostasis in depressed patients. Persistence of hypersomnolence after

depressive symptoms have been adequately treated may signal risk for recurrent depression (Breslau, Roth, Rosenthal, & Andreski, 1996; Roberts, Shema, Kaplan, & Strawbridge, 2000).

A diagnosis of Kleine–Levin syndrome should be considered among hypersomnolent patients. This neurological disorder is characterized by recurring periods of hypersomnolence lasting several weeks to several months. These individuals demonstrate largely normal cognitive, emotional, and behavioral functions between episodes. Patients with Kleine-Levin hypersomnia often demonstrate compulsive eating (polyphagia), inappropriate sexuality (e.g., public masturbation), or other bizarre behaviors during episodes. Patients with recurrent hypersomnia are much more likely to demonstrate neurological problems such as impaired memory, gait disturbances, and autonomic nervous system dysfunctions (e.g., sweating, flushing, low blood pressure, and bradycardia) (Billiard, Jaussent, Dauvilliers, & Besset, 2011).

Breathing-related sleep disorders (i.e., obstructive sleep apnea) must also be ruled out. These are serious conditions that, when left untreated, lead to impaired memory and work performance, poor motor coordination, poor executive functions, and health risks. Risk factors are obesity, large neck circumference (> 17 inches), increasing age (over 40% in the elderly), male gender, positive family history, or any medical condition that obstructs or impairs the patency of the upper airway. However, normal or even underweight individuals can be diagnosed with obstructive sleep apnea. Although PSG is required to diagnose a breathing-related sleep disorder, excessive daytime sleepiness, loud snoring or gasping during sleep, dry mouth upon waking, and recurrent headaches are cardinal features.

Narcolepsy commonly co-occurs with depressive symptoms. A precise causal relationship remains unclear but bidirectional associations are suggested. For example, hypocretin deficiency, through a cholinergic–monoaminergic imbalance, is linked with dysregulation of mood (Dauvilliers, Lopez, Ohayan, & Bayard, 2013). Like narcoleptics, patients with MDD or patients in the depressed phase of bipolar disorder commonly experience fatigue and excessive daytime sleepiness. Mood disorders also can be associated with psychosis, and hypnagogic/hypnopompic hallucinations associated with narcolepsy may be interpreted as psychotic symptoms.

Because circadian rhythm sleep-wake disorders include problems remaining alert or sleeping at appropriate times, differentiation from disorders of inadequate or excessive sleep should be made. *DSM-5* recognizes three subtypes of circadian rhythm sleep-wake disorders including delayed sleep phase type (most common in adolescents), advanced sleep phase type (most common in older and geriatric patients), and irregular sleep-wake type. The essential characteristic of these disorders is a misalignment between the required/desired sleep schedule and natural biological rhythms.

Individuals with restless legs syndrome have symptoms (e.g., creepy-crawly feelings in the legs) that commonly interfere with sleep. There are clear-cut urges to physically get up and move around, which temporarily reduces "tension" in the legs. A high proportion (up to 75%) of patients with restless legs syndrome develop repeated limb movements in sleep, which are characterized by muscle twitches and jerks every 20–40 seconds throughout the night. Since restless legs syndrome is commonly associated with sleep-related periodic limb movements (PLMs),

insomnia and hypersomnia complaints are common since movements may occur hundreds of times throughout the night and disrupt sleep.

Psychological and Biological Assessment

Polysomnography (PSG) is not generally used as a tool in the diagnosis of insomnia. No objective findings on PSG (e.g., sleep architecture, proportion of time in sleep stages) are specific to insomnia. Subjective sleep logs and/or actigraphy are commonly used; however, there is lack of consensus regarding quantitative criteria for identifying insomnia. Somewhat arbitrarily, difficulty initiating sleep is often defined by subjective sleep latency of greater than 20–30 minutes, whereas difficulty maintaining sleep has been defined by subjective time awake after sleep onset greater than 20–30 minutes. Research has suggested that a useful combination of actigraphic sleep parameters to assess insomnia include total sleep time, sleep onset latency, and number of awakenings longer than 5 minutes (Natale, Plazzi, & Martoni, 2009).

In hypersomnolent patients, the PSG will typically show decreased sleep latency, increased total sleep time, and normal (or increased) sleep efficiency. The amount of time in deep sleep may be increased. The average MSLT sleep latency is short (<5 minutes). Kleine-Levin hypersomnia is associated with increased sleep propensity on MSLT. A distinctive PSG feature of narcolepsy is sleep-onset REM. The first REM period in healthy individuals takes place about 90 minutes after sleep onset. In patients with narcolepsy, the first REM period often takes place in less than 20 minutes or, in some cases, "the moment the head hits the pillow"; thus, the term sleep-onset REM. Sleep-onset REM also may take place during daytime naps, particularly in those narcoleptic patients with sleep deprivation.

Although the presence of sleep-onset REM on the MSLT is highly suggestive of narcolepsy, it is not a definitive confirmation of the disorder (Mignot et al., 2002). Since most narcoleptic patients are hypocretin deficient (i.e., low levels or the absence of hypocretin in CSF) (Mignot et al., 2002), measuring CSF hypocretin-1 is considered a definitive diagnostic test. It is often most useful in cases where MSLT findings are difficult to interpret.

If there are no identified mechanical blockages (e.g., enlarged tonsils or craniofacial abnormalities) or endocrine disorders, continuous positive airway pressure (CPAP) is the treatment of choice for obstructive sleep apnea. CPAP is highly effective but associated with poor compliance, which can be attributed to the cumbersome and noisy nature of the equipment. Concomitant cognitive-behavioral or motivational interventions may be successful in improving CPAP compliance problems.

There is no diagnostic test for circadian rhythm sleep-wake disorders. A history of external changes in the timing of sleep in conjunction with a sleep log or actigraphy makes it fairly easy to identify circadian disorders. Individuals with a delayed sleep phase almost always report having extreme difficulty waking in the morning, whereas the individual with an advanced sleep phase will report difficulty maintaining wakefulness during the evening hours.

The diagnosis of restless legs syndrome is made on the basis of history and ruling out other possible medical or neurological diseases. Talking with the patient's bed partner is valuable, because this person will inevitably report extreme restlessness throughout the night, which is easily confirmed by polysomnography. Patients with

restless legs syndrome often meet ICSD-2 criteria for periodic limb movement disorder (PLMD), which can be confirmed with overnight PSG.

Etiological Considerations

Up to 50% of insomnia patients meet criteria for a comorbid mental health diagnosis, most commonly anxiety or depression. Research suggests this relationship to be reciprocal: Insomnia increases risk for medical/psychiatric conditions and medical/psychiatric conditions increase insomnia risk. Onset of insomnia in childhood is prognostic for later mental illness and persistent sleep problems into adulthood (Ford & Kamerow, 1989; Ohayon et al., 1998). Precise mechanistic pathways remain poorly understood, but several neurotransmitter systems (e.g., noradrenergic, GABAergic, serotonergic, and hypocretinergic) are involved in the regulation of arousal.

Some individuals with hypersomnolence disorder have a family history of the disorder and there is an autosomal dominant mode of inheritance. Viral infections, including infectious mononucleosis, can sometimes evolve into hypersomnolence in the months following infection. Hypersomnolence following a traumatic brain injury can persist up to one year, and acute psychological stress can be followed by a period of hypersomnolence. Lesions in the frontal and occipital lobes, hippocampus, amygdala, and pontine locus coeruleus have been associated with hypersomnia, as well inappropriate sexual behaviors and compulsive eating.

First-degree relatives of probands with narcolepsy have an increased risk compared to relatives of unaffected probands. However, only 25% of monozygotic twins are concordant for narcolepsy, which suggests a strong environmental influence. Human leukocyte antigen susceptibility factors for narcolepsy (HLA-DR2 and HLA-DQB1*0602) and low cerebrospinal fluid levels of hypocretin-1 in narcoleptics with cataplexy are well-established (Lin & Mignot, 2007; Mignot et al., 2002). There also appears to be a loss of hypothalamic hypocretinergic neurons in postmortem patients with narcolepsy (Blouin et al., 2005). The hypocretin neurotransmitter system is largely excitatory and stimulates neuronal activity in multiple projection areas in the brain, including interfacing with acetylcholine and noradrenergic (i.e., locus ceruleus) nuclei, which are, respectively, involved in REM and muscle atonia.

More than 86% of obese patients with type 2 diabetes have a breathing-related sleep disorder (Foster et al., 2009), and overweight and obese people report getting less sleep than do patients of normal weight. Nordin and Kaplan (2010) found that complaints of sleep initiation or maintaining sleep are a predictor of significant weight gain when tracked over an approximately 29-year period of time. Thus, there appears to be a bidirectional relationship between insomnia and obesity. It is possible that the early diagnosis and treatment of insomnia will prevent the later sequential development of obesity, obstructive sleep apnea, and sleep deprivation–related neurological impairments.

A person's desire and ability to fall asleep are influenced by both the length of time since the last sleep period and by internal circadian rhythms. Thus, the body is ready for sleep and for wakefulness at different times of the day. Circadian rhythm sleep-wake disorders are caused by an inadequate ability to reset the sleep/wake cycle in

response to environmental time cues. Shift work, time zone changes, certain medications, and changes in routines can result in circadian disorders.

The familial pattern of restless legs syndrome has been appreciated since its first description by Ekbom (1944). There is an approximately 83% concordance in monozygotic twins. Desautels and coworkers (2001) identified the first locus linked to restless legs syndrome on chromosome 12. More recently, other genes and loci have been linked to restless legs syndrome. Pathophysiologic mechanisms include abnormalities in the dopaminergic system and iron metabolism.

Course and Prognosis

The thorny issue for clinicians is what to do with patients who suffer from insomnia or hypersomnolence that could be caused by an underlying medical, psychiatric, or other sleep disorder. In theory, if the underlying disease is effectively treated, then the sleep problem should resolve. When this is the case, it is justified to focus exclusively on the underlying medical, psychiatric, or other sleep condition (e.g., obstructive sleep apnea). Often, however, conclusions are less definitive. Even dramatic improvements in the underlying medical (e.g., fibromyalgia), sleep (e.g., obstructive sleep apnea), or psychiatric (e.g., major depression) condition may not be associated with parallel improvements in the insomnia or hypersomnia. In such situations, the patient requires separate treatment for the sleep problem and would receive a sleep diagnosis. Most importantly, the patient should receive targeted and comprehensive treatment for *both* the sleep disorder and any other coexisting disorder(s) toward improving the long-term course, prognosis, and outcomes.

PARASOMNIAS

According to *DSM-5,* parasomnias are characterized by abnormal behavioral, experiential, or physiological events that occur in association with sleep or emerge during a specific sleep stage (e.g., REM behavior disorder) or during sleep-wake transitions. The most common parasomnias, including non-REM sleep arousal disorders and REM sleep behavior disorder, represent admixtures of wake and sleep. Patients with parasomnias often come to the attention of mental health providers due to their associated bizarre, wild, and sometimes dangerous behaviors. Serious self-inflicted injuries and aggression, including homicidal behaviors, have been linked to parasomnias.

Nightmare Disorder

Nightmare disorder occurs almost exclusively during rapid eye movement (REM) sleep and thus is more likely to occur during the second half of the nighttime sleep period. Nightmares are characterized by repeated occurrences of lengthy and realistic sequences of dream imagery that elicit anxiety, fear, and other negative emotions. Once awakened, the individual quickly becomes oriented, alert, and remembers the dream in detail. However, negative emotions may persist and contribute to subsequent problems initiating sleep.

Epidemiology and Other Features All people experience bad dreams or nightmares. They are particularly common during childhood, with approximately 25% of school-aged children experiencing a nightmare at least once per week. Prevalence rates decrease steadily with age; about 6% of adults experience at least one nightmare per week and only 1%–2% experience more frequent nightmares. The peak ages for experiencing "distressing" nightmares are 10–29 for women and 30–49 for men (Nielsen, 2010).

The experience of a single nightmare or even several nightmares is not itself indicative of a sleep disorder and/or the need for treatment. Typically, the content of nightmares revolves around imminent harm being caused to the individual (e.g., being chased, threatened, etc.). Nightmares commonly occur in the context of post-traumatic stress disorder (PTSD) and tend to involve the original traumatic event. Frequent nightmares, particularly if they are coupled with full awakenings and delayed return to sleep, may produce clinically significant insomnia.

Non-REM Sleep Arousal Disorders

Non-REM Sleep Arousal Disorders are characterized by the repeated occurrence of incomplete arousals from non-REM sleep. Thus, arousals typically occur during the first third of the nighttime sleep episode. They are typically brief in duration (e.g., 10 minutes) but may last up to 1 hour. Two major types of non-REM Sleep Arousal Disorders are described in *DSM-5:* sleep terrors and sleepwalking.

Sleep terrors (also called night terrors) are characterized by repeated arousals from sleep, which are heralded by yelling, screaming, or crying. The person appears frightened. It is very difficult for an observer to awaken the person and terminate the episode. There is no dream recall and, in fact, there is amnesia for the event upon awakening to full consciousness the next day. There must be evidence of significant clinical distress or impairment as a consequence of these events, which cannot be exclusively attributed to another medical, substance, or mental disorder.

Sleepwalking is characterized by its namesake (i.e., repeated complex motor behaviors that involve getting out of bed and walking around). Like sleep terrors, there is amnesia the next morning about the event. During the events themselves, which may last from a few minutes to as long as 30–45 minutes, the individual often has a blank stare and does not appear to be aware of his or her surroundings. Similar to sleep terror events, the patient is very difficult to awaken or terminate the episode. Sleep-related eating or sexual behavior may occur during sleepwalking episodes.

Epidemiology and Other Features Non-REM Sleep Arousal Disorders are not infrequent in the general population. Between 10% and 30% of children have had at least one sleepwalking episode and 2% sleepwalk often. Prevalence of sleepwalking episodes in adults is lower (1%–7%), corresponding with a normal reduction in non-REM sleep in adulthood. Similarly, sleep terrors are more common in children as compared to adults. Prevalence in young children is around 20% with approximately 4%–5% experiencing an episode once or more a week.

Patients with sleepwalking can later develop sleep terrors or vice versa, and both sleep terrors and sleepwalking can coexist within the same episode. Children who develop sleep terrors before the age of 10 are more likely to suffer from sleep

terrors in adulthood, and up to 75% of patients with sleep terrors will report sleepwalking. Among patients who sleepwalk, safety precautions should be taken since, although rare, some sleepwalkers may leave their house and/or injure themselves during an episode.

Notable accompanying features of sleep terrors include signs of extreme autonomic arousal including tachycardia, rapid breathing, sweating, and pupil dilation. Because the individual may sit up in bed with their eyes open, sleep terrors may be mistaken for nightmares. However, unlike a nightmare, there will be amnesia for the event the following day. Sleep terrors rarely arise during daytime naps.

REM Sleep Behavior Disorder

REM behavior disorder, as indicated by its name, is a disorder of REM sleep including repeated episodes of arousal typically associated with vocalizations and/or complex motor behaviors (APA, 2013). Behaviors often reflect motor responses to the content of action-filled or violent dreams. Thus, although behaviors may appear bizarre, on close examination they often make sense when understood within the context of the dream content. A fundamental feature of this type of parasomnia is an absence of the muscle paralysis that is normally associated with REM-stage sleep (i.e., there is REM without muscle atonia). Behaviors may range from mild hand movements or facial expressions to very complex motor behaviors. There appear to be strong emotions (e.g., rage, anger) associated with many of these behaviors.

Epidemiology and Other Features REM sleep behavior disorder usually appears for the first time in adulthood, although it has been reported in childhood. Most information comes from clinical samples with a high male predominance. Men over the age of 50 are most likely to be affected. When the diagnosis is made in younger individuals, particularly those without coexisting neurological problems, there is close to a 1:1 gender ratio. The best available information suggests an approximate prevalence of 0.5% in the general population.

Unlike patients with non-REM sleep arousal disorders, patients with REM sleep behavior disorder are often able to recall dream content upon awakening. This disorder is usually noticed when it causes danger to the patient, their bed partner, or others they encounter. Negative effects such as injury to the self or bed partner sustained during an episode precede diagnosis. Thus, an important aspect of management of patients is environmental safety. Comorbid narcolepsy occurs in approximately 30% of cases and, consistent with the demographic profile of narcolepsy, these patients are typically younger in age.

Diagnostic Considerations

To a large extent, a person is defined as having nightmare disorder when he or she experiences great distress and/or is impaired by the episodes. Distressing nightmares are common following a traumatic event and represent hallmark features of PTSD. The content of PTSD-related nightmares often contains features of the original trauma, including the experience of reliving the traumatic event (Mellman & Hipolito, 2006). However, not all nightmares that occur after a trauma are a direct replay of the event.

People with PTSD are more likely to have dreams that are exact replays of the event than are trauma-exposed individuals without PTSD. Some research has shown that nightmares following a trauma may occur earlier in the night and during different stages of sleep as compared to nightmares in general. They may also include a greater number of body movements.

Unlike non-REM and REM-based sleep arousals, individuals with nightmares are fully alert and aware of their surroundings after awakening. And, unlike sleep paralysis, nightmares are easily identified as unreal events. Nightmares in children are nonetheless often confused with sleep terrors by parents. The child with sleep terrors has no recollection of the episode; the only memory associated with sleep terrors may be the image of a parent vigorously attempting to awaken the child from sleep. Sleep terrors are less prevalent in adults but can also be distinguished by amnesia for the episode. Nightmares in children are linked to high levels of anxiety, anxiety proneness, and/or stressful events (Beidel & Alfano, 2011) whereas this is not necessarily the case in adults. In both children and adults with nightmares, a history of trauma and possible PTSD should be considered.

Non-REM and REM-based sleep disorders may be conceptualized as a transient, sleep-related uncoupling of higher cognitive functions from intact motor behaviors. It is not unusual for an individual with one type of parasomnia to suffer from a second or even third type. Some investigators view sleep terrors and sleepwalking as clinical variants of a common diathesis. This view is supported by (a) high comorbidity of sleepwalking in patients with sleep terror disorder; (b) children with sleep terrors often become adult sleepwalkers; and (c) sleep terrors and sleepwalking often co-occur in the same sleep event. Sleep-related seizures should be considered in the differential diagnosis.

Non-REM sleep arousal disorders may include a range of sexual behaviors (e.g., masturbation, intercourse). These behaviors are often abrupt in onset and appear senseless and without motivation or purpose. The sexual behaviors are often outside the norm for the individual compared to his or her sexual activities during waking, fully conscious states. The sexual acts can be aggressive in nature, reflecting rape, sadomasochistic, or humiliating motifs. Actions tend to develop abruptly during partial awakenings after one or more hours of sleep. There is amnesia for the events accompanied by a sense of guilt, shame, or disgust upon realization of the sexual acts.

In patients exhibiting sexual behaviors associated with sleep, Kleine-Levin syndrome along with seizure disorders should be ruled out. Sexual gestures, body thrusts, sexual moaning, and other sexual-like automatisms have been associated with seizure disorders including frontal and temporal lobe pathology. However, episodes taking place during both waking and sleeping states and that have focal or stereotypical motor behaviors are associated with seizures and not parasomnias (Nickell & Uhde, 1991). The sun-downing phenomenon needs to be considered in the elderly, in whom apparent disorientation and/or walking around aimlessly is reported. Finally, malingering should be part of the differential diagnosis as well, especially when the patient has been charged with a crime or has a history of sociopathy and a sleep disorder diagnosis might be leveraged to his/her advantage.

Sleep paralysis is characterized by a discrete period of time during which voluntary muscle movement is inhibited, yet ocular and respiratory movements are intact. The symptoms of recurrent sleep paralysis are, in most cases, easily distinguished from

other parasomnias. The main challenge is to determine whether there is additional evidence of cataplexy and excessive daytime drowsiness to justify a diagnosis of narcolepsy. Although both sleep paralysis and panic attacks arising from sleep are frightening, sleep panic attacks are not associated with muscle paralysis. Also, patients with sleep panic attacks do not report visitation experiences and/or report hypnagogic or hypnopompic hallucinations. Time misperception is commonly associated with sleep paralysis. Specifically, experiential time during sleep paralytic events is often much greater than actual clock time. Neither sleep paralysis nor sleep panic attacks are accompanied by amnesia, confusional arousals, or clouding of consciousness.

Sleep panic attacks are fearful arousals from sleep lasting up to several minutes. Sleep panic attacks are non-REM events, which typically take place during one of the first two non-REM cycles. However, unlike other types of arousals from non-REM sleep, sleep panic attacks are associated with complete awakenings to full alertness. The next morning, patients have full and accurate recall of the previous night's panic attacks. There are no dreams, vivid images, or cognitions during sleep panic attacks. Instead, they are characterized by profound fear and frequently (but not always) physiological hyperarousal (e.g., tachycardia, increased respiratory rate, increased blood pressure), but changes in heart and respiratory rate are less impressive than those observed in sleep terror disorder. After awakening, patients may develop fear-related cognitions, with content focused on worries about death and dying. As few as one sleep panic attack can lead to secondary (i.e., conditioned or context-specific) sleep-based avoidance behaviors.

PSYCHOLOGICAL AND BIOLOGICAL ASSESSMENT

Patients with recurrent nightmares tend to experience decreased frequency and severity of nightmares when they are studied in the sleep laboratory environment. This improvement is attributed to the positive impact of safety cues (i.e., being monitored by staff and physicians). Nightmare sufferers do not demonstrate impressive differences from healthy normal controls on measures of sleep onset latency or sleep efficiency. Increased gross motor activity is sometimes observed in individuals with frequent nightmares.

Hypersynchronous slow-wave EEG activity may develop just before a sleep terror with the rapid appearance of a waking EEG pattern (Broughton, 1968). Increased fragmented sleep with multiple arousals during delta sleep is associated with sleep terrors and sleepwalking. Sleepwalkers have decreased EEG power in the delta band (0.75–4.5 Hz), with the most significant difference between sleepwalkers and normal controls being in the first non-REM cycle. Other lines of evidence in sleepwalkers suggest that after partial arousals there may be high-voltage theta/delta mixed in with alpha and beta wave activity.

REM sleep behavior disorder symptoms tend to take place during the second half of the sleep cycle when REM is predominant. Because this is a condition characterized by REM sleep without muscle paralysis, the diagnosis can be easily established by combining PSG with careful video monitoring. Extra EMG leads should be placed on different muscle groups of the body, because only selective areas may be associated with increased muscle tone, activity, or frank movement (e.g., arms but not legs). Patients with recent-onset REM behavior without atonia should receive a careful

documentation of their course of illness, with a comprehensive workup including polysomnography with EEG synchronized video recording.

The belief that sleep paralysis is a REM-related event is mainly based upon extrapolations from patients' self-reports. Two peak time periods, including within the first 2 hours of sleep and during early morning sleep have been reported (Cheyne, 2002; Girard & Cheyne, 2006). However, sleep paralysis episodes can take place at any point throughout the sleep night. Some evidence suggests that sleep paralysis can be induced in prone individuals by interrupting the first REM period.

The physiology of sleep paralysis is similar to cataplexy insofar as both phenomena are characterized by muscle atonia. However, one condition (sleep paralysis) emerges during transitions into and/or out of sleep whereas the other (cataplexy) takes place during alert wakefulness. Both sleep paralysis and cataplexy, together with hallucinations and excessive daytime drowsiness, are components of the so-called narcoleptic tetrad.

Sleep panic attacks occur during the first half of the sleep period, and almost always within 3 hours of sleep onset (Craske & Barlow, 1989; Mellman & Uhde, 1988). Sleep panic attacks are abrupt awakenings and almost always emerge during the transition from late N2 to early N3 sleep (Mellman & Uhde, 1988; Uhde, 2000). There is no seizure activity on EEG, although sleep-related seizures can be associated with anxiety or even panic-like episodes (Nickell & Uhde, 1991). Thus, sleep-related seizures are part of the differential diagnosis of sleep panic attacks. As a consequence of developing a conditioned fear of sleep, many patients with sleep panic attacks will have prolonged sleep latencies, decreased sleep efficiencies, and decreased total sleep times. However, these findings are not consistent across all studies, and there is a subgroup with sleep state misperception.

Etiological Considerations

A good portion of research examining the etiology of nightmares has focused on children with findings suggestive of an interaction between genetic and environmental factors (King, Hamilton, & Ollendick, 1988). A significant relationship between increased levels of trait anxiety and nightmares also has been proposed to reflect the fact that increased levels of anxiety both result from and are a predisposing factor for nightmares (Mindell & Barrett, 2002). Genetic influence on nightmares has been found to account for an estimated 45% of the phenotypic variance in childhood, and for an estimated 37% in adulthood (Hublin, Kaprio, Partinen, & Koskenvuo, 1999). Traumatic events, psychological distress, or other sleep disturbances may contribute to the onset and maintenance of nightmares as well.

Pedigree studies suggest a very high rate of heritability for sleep terrors (Kales et al., 1980), and there is a strong heritability associated with sleep terror and sleepwalking comorbidity. Probands with a positive sleepwalking history have a 5- to 10-fold greater concordance for sleepwalking in monozygotic compared to dizygotic twins. Sleep deprivation, stressful life events/changes, high fevers, light or noise in the environment, and certain medications (e.g., sedatives) appear to be triggers for sleep terrors and sleepwalking episodes, although specific mechanisms are not well understood.

At present there is no genetic test for REM sleep behavior disorder, either as a primary condition or complication of other medical conditions associated with REM

without atonia. Selective lesions of subnuclei in the reticular formation and the locus ceruleus, as well as pure pontine infarctions in humans, are known to produce REM behaviors without atonia. These observations support brainstem abnormalities in the underlying pathophysiology.

REM sleep behavior disorder may present years in advance of multiple system atrophy and Parkinson's disease, disorders characterized in part by abnormal accumulations of alpha-synucelein that destroy dopamine-producing cells. Findings from animal and human studies suggest that lesions or dysfunction in REM sleep and motor control circuitry in the pontomedullary structures cause REM sleep behavior disorder. Early degeneration of these structures is hypothesized to explain the presence of REM sleep-behavior disorder years or decades before the onset of neurodegenerative disease (Boeve, 2013).

Course and Prognosis

Unlike patients with sleep panic attacks, most patients with nightmares do not develop a fear of sleeping. Both the degree of distress and frequency of nightmares are employed as guideposts in making treatment decisions, but neither of these constructs are well-established predictors of treatment response. Some data suggest that the preexisting level of waking psychological disturbance or neuroticism, rather than the frequency of nightmares per se, is most likely to predict distress and/or impairment from nightmares (Belicki, 1992).

In terms of nightmares associated with life-threatening events or situations that threaten bodily integrity, the natural course is an initial peak in trauma-related nightmares followed by a progressive decrease and then disappearance over several months. Within the context of PTSD-related nightmares, those individuals whose nightmares fail to extinguish over several months ultimately require treatment. It is not possible at present to predict who will or will not follow a positive extinction versus nonextinction pattern, and ability to provide early interventions after a traumatic exposure is therefore limited. Individuals with persistent PTSD-related nightmares will likely show dysfunctions in other areas of work, social, and interpersonal performance. In both children and adults, with or without known antecedent traumatic exposures, evidence of ongoing fear of sleep/sleeping or intense distresses about dream content are reasonable indications for treatment.

Injuries incurred during sleepwalking episodes may include bone fractures, lacerations, walking into walls, and aggressive behaviors toward others. Sleepwalkers appear confused and disoriented when engaged in activities, which range from simple tasks such as hand gestures or turning on a bedside lamp to quite complex behaviors such as walking down the street to an all-night deli and ordering food. Episodes may last from a few seconds to up to 30–40 minutes. The behaviors undertaken by sleepwalkers are frequently out of character, and there is confusion immediately after awakening with a lack of memory for the sleepwalking events. Sleepwalking may or may not reduce with age. It usually does not indicate a serious disorder, although it can be a symptom of other disorders.

Unlike patients with sleep terrors or other confusional states that arise from deep sleep, patients with REM sleep behavior disorder tend to remain in the bed (or in the area where they were sleeping) when they act out dreams. An exact diagnosis of

idiopathic REM behavior disorder is often challenging, because REM-related behaviors without atonia often coexist with confusional arousal disorders, narcolepsy, and neurodegenerative diseases. There is evidence that REM without atonia is an early marker of neurodegenerative diseases such as Parkinson's disease and multiple system atrophy, which may emerge 10 or more years later (Mahowald, Bramer Bornemann, & Schenck, 2010). In some cases, symptoms of REM sleep without atonia may herald the onset of narcolepsy.

Tricyclic, serotonin selective reuptake inhibitor (SSRI), and serotonin-norepinephrine reuptake inhibitor (SNRI) antidepressants may induce and worsen preexisting symptoms of REM sleep behavior disorder. In patients with violent behaviors, there may be self-injury or injuries inflicted on the bed partner. As one might imagine, the bed partner may become extremely frightened of the person with REM sleep behavior disorder. In patients with violent behaviors, there is a risk of serious, even life-threatening injuries. Patients should be evaluated for the presence of coexisting neurological disorders (i.e., seizures and neurodegenerative disorders) as well as the use of psychotropic medications. Because the motor manifestation of REM sleep behavior disorder can be frightening and/or dangerous, it is useful to tell the patient and his or her family that the person is taking actions that would be appropriate if the dreams were real events.

Initial episodes of sleep paralysis are unequivocally frightening. There is almost always a fight-or-flight response, although with sleep paralysis the person can neither put up a defense nor flee the situation. This realization only magnifies the fear and causes a sense of total vulnerability. Some individuals recognize the paralysis as a true physiological state of muscle weakness, whereas others report being "controlled by an evil force" or "frozen with fear." Sleep paralysis ranges in frequency from a single lifetime episode to multiple episodes in a single night. Similar to patients with panic attacks, the frequency of paralytic events does not strongly predict the degree of psychological distress. Unlike patients with sleep panic attacks, it is unusual for patients with recurrent sleep paralysis to develop a conditioned fear of sleep.

The cultural background and heritage of the patient are particularly relevant in treating sleep paralysis. The depiction of the "evil presence" is remarkably similar across cultures, even among people who had no prior knowledge of the phenomenon (for a superb review, see Hufford, 1982). The hypnagogic/hypnopompic "visitor" is often an old woman who has been given various names (e.g., old hag, succubus) to describe the associated experience ("being held down by ghosts," "witch riding my back," "sucking the breath out of me"). Patients from Western and/or European backgrounds are exceedingly cautious about telling anyone, especially mental health professionals, about their hallucination-related visitation experiences. Patients are relieved to talk with a mental health professional who is knowledgeable about the syndrome. Education is a core element of treatment.

Up to one-third of patients with diagnosed panic disorder report nocturnal panic attacks. Several lines of evidence suggest important differences between panic patients with and without sleep panic attacks. For example, sleep panic attacks may be more often associated with trauma (Freed, Craske, & Greher, 1999), comorbid depression (Agaragun & Kara, 1998; Uhde, 2000), and more restricted sleep patterns (i.e., less than 5 hours of sleep per night) (Singareddy & Uhde, 2009).

Patients with sex-related non-REM sleep arousal disorders who wish to prevent dangerous or aggressive sleep-related behaviors should be made aware of and avoid possible predisposing conditions such as alcohol, medications, or other substances. Education is a major component of treatment. It is helpful to educate patients and families about sleep-wake mechanisms involved in the parasomnias. It is common for family members to believe that sleepwalking, sleep-related sexual behaviors, REM-related sleep aggression, and other disturbing parasomnias are under the direct conscious control of the patient. Good sleep hygiene (particularly avoiding sleep deprivation) and maintaining a safe sleep environment (i.e., eliminating situations such as open windows that increase the risk of physical harm) should be incorporated into the management of parasomnias. There is a tendency to try to awaken the person out of a confusional state. This is often a mistake because attempts to interrupt sleep may only worsen the situation.

CASE STUDY

BACKGROUND AND HISTORY

Ms. Case is a 30-year-old married, normal weight African-American woman with an 8-year history of panic disorder with agoraphobia. Her first daytime panic attack occurred while shopping. There were no major life stressors at the time. She described her first lifetime panic attack as "out of the blue" and "not like anything I'd ever experienced before." She had 15 panic attacks over the next 2 months, always while she was fully awake. These attacks were characterized by tachycardia, chest tightness, sweating (over her lip and hands), and a strange feeling of floating and "time standing still." During this first wake episode she thought she was dying from a heart attack. Her medical and neurological workup was negative. The ER physician prescribed a medication for her anxiety but she was noncompliant ("I didn't want to put drugs in my body"). She later worked with a therapist. This was helpful in dealing with what she perceived as minor family issues (e.g., her husband was complaining that she never wanted to do anything fun anymore).

Over the next several years, her wake panic attacks decreased in frequency and she learned "how to handle them." Now and then, usually after the flu or a limited-symptom panic attack, she would become a "little concerned" about having another attack, but no avoidance behaviors were described. However, these minor concerns became extreme, including nonstop thoughts about "going crazy" or dying after she experienced her first of many subsequent sleep panic attacks. Ms. Case perceived her sleep panic attacks as more unpredictable and serious than her wake panic attacks. Her sleep panic symptoms were very similar to her wake panic attacks, which re-emerged with greater frequency and included a pounding heart, numbness in her hands, choking, and feeling unreal. She also reported being hot and sweating and fearful that she had a serious medical illness. What made her most afraid, however, was her inability to catch her breath, particularly at night. Ms. Case developed a fear of sleep, which resulted in maladaptive sleep habits (e.g., sleeping in a chair rather than the bed and making her husband promise to watch her sleep in order to wake her up if she stopped breathing). The husband reported that he had never witnessed his wife stop breathing and that she snored only when she had a cold. The patient's fear of

sleep led to a pattern of insomnia, with fragmented sleep and periods of sleep deprivation lasting up to 24 hours.

The patient also had a history of nightmares. Her sleep panic attacks, however, were qualitatively different from her nightmares (i.e., there was no dream content or visual images associated with her panic attacks) and her nightmares caused no distress or impairment. She also reported a history since childhood of isolated episodes of sleep paralysis. While she remembers these intermittent childhood events as frightening, she no longer considered them distressing.

Because of Ms. Case's concerns about breathing, she obtained an overnight sleep study. Except for some difficulty falling asleep (i.e., her sleep onset latency was 30 minutes), she did not experience any type of frightening arousal while studied in the sleep lab. All results were well within normal limits. She also reported that she slept better in the sleep lab than she slept at home.

Diagnostic Conceptualization

This case illustrates the value of (a) obtaining a longitudinal perspective; (b) determining the degree of distress and impact of the patient's sleep complaints on work, social, and other important areas of function; and (c) appraising the merits of treating the sleep problem(s) as a distinct disorder(s). Despite a waxing and waning of daytime symptoms, this individual clearly suffers from long-standing panic. Although the wake panic attacks may have decreased in frequency for a period of time and the associated avoidance behaviors were downplayed by the patient, it would be a mistake to ignore the negative impact of wake panic attacks on this person's overall health and well-being. Thus, she meets criteria for *DSM-5* panic disorder (300.01).

The emergence of sleep panic attacks after years of having wake panic attacks presents a diagnostic dilemma. One could view the presence of sleep panic attacks in this case as just a symptom variant of panic disorder. This viewpoint argues for a single diagnosis of panic. However, a single diagnosis might unwittingly lead some clinicians to presume that the use of well-established, empirically supported treatments for panic disorder will be adequately effective in managing sleep panic attacks and associated symptoms. Although this may be the case for some patients, Ms. Case's maladaptive sleep habits and fragmented sleep patterns clearly warrant direct clinical attention. A separate sleep disorder diagnosis, therefore, is justified.

So what is the appropriate sleep disorder diagnosis? *DSM-5* describes the frequent presence of nocturnal panic attacks in panic disorder patients and associated fears related to health and well-being. However, in this case, the patients' persistent problems with sleep initiation/maintenance and maladaptive sleep behaviors resulted in an overall insufficient amount of sleep and associated impairment. From this standpoint, an additional diagnosis of insomnia disorder (780.52) would be appropriate. Notably, inadequate sleep is a trigger for the recrudescence and severity of panic attacks (Uhde, 2000).

Notably, *DSM-5* does not provide guidelines for the diagnosis of individuals who experience nocturnal panic attacks in the absence of wake panic attacks. If our patient no longer experienced daytime panic attacks or avoidance, it would be justified to give a diagnosis of other specified anxiety disorder (300.09), in addition to an insomnia diagnosis, in light of her significant and impairing fears related to sleep and breathing at

night. Our patient did report a history of nightmares; however, insufficient information was provided to ascertain whether Ms. Case would have met criteria for nightmare disorder (307.47) in the past, but she clearly was not distressed or disturbed by dreams at the time of evaluation, nor was there any evidence for interpersonal, social, or occupational impairment related to her dream experiences. The same is true of the patient's report of sleep paralysis. Also, no information was provided regarding a history of sexual, physical, or life-threatening trauma, which would have been critical information in the event that her nightmares did cause significant distress or impairment.

Even though Ms. Case had a normal body mass index (BMI) and snored only when sick, it was appropriate to obtain an overnight PSG to rule out a breathing-related sleep disorder. Normal-weight, nonsnoring people can suffer from obstructive sleep apnea, and the absence of these clinical features should not be used to rule out a breathing-related sleep disorder. If there had been objective evidence of sleep apnea during her PSG, which there was not for this patient, then a breathing-related sleep disorder would be added as another Axis I disorder and listed as a medical condition on Axis III.

SUMMARY

A considerably expanded list of sleep disorders in *DSM-5* reflects an attempt to enhance the clinical utility of definitions and diagnostic criteria for general medical or mental health clinicians and to clarify when referral is appropriate to a sleep specialist. Among a host of revisions, several specific changes are noteworthy. First, removal of two previous diagnoses, namely, sleep disorder related to another mental disorder and sleep disorder related to another medical condition, underscores a need for independent clinical attention toward sleep disorders regardless of other mental or medical problems that may be present. Along these lines, a change from *primary insomnia* (*DSM-IV*) to *insomnia disorder (DSM-5)* is specifically intended to avoid a primary versus secondary designation of the disorder when it co-occurs with other conditions.

Second, *DSM-5* distinguishes narcolepsy, now well-known to be associated with hypocretin deficiency, from other forms of hypersomnolence. These changes reflect burgeoning neurobiological and genetic evidence from sleep-based research. Finally, age-dependent variations in the presentation and course of sleep-wake disorders are included as available. This developmental perspective recognizes that pediatric (in addition to adult) sleep-wake disorders are highly common phenomena and that sleep health is critical across all stages of the life-span.

Overall, sleep-wake disorders range considerably in their presentation, course, and underlying pathophysiology. Comprehensive assessment, which may include a detailed patient history, physical exam, completion of questionnaires and sleep diaries, and/or objective sleep measures are required. Effective treatments are similarly varied and may include behavioral, pharmacologic, and/or other treatments in combination with psychiatric or medical care. However, a common challenge encountered by clinicians is eliminating other possible causes of sleep symptoms. This is not always easy, as there are many common symptoms within and across the sleep-wake disorders alone, and high rates of comorbidity are the rule rather than the exception.

One of the most valuable tools for understanding the symptoms and course of a sleep disorder when other problems/conditions are present is to use life-charting methods to plot the temporal relationship among major life events, medical illnesses, sleep symptoms, and mood (Roy-Byrne, Post, Uhde, Porcu, & Davis, 1985; Uhde et al., 1985). It is also critical to assess the history of medications, alcohol, and other substances over the entire lifetime of the individual. The life-charting strategy often uncovers important relationships that were previously unrecognized by both the patient and the clinician (Roy-Byrne et al., 1985). Although this approach has not been validated in patients with sleep-wake disorders per se, there is strong evidence for its utility in the assessment of complex psychiatric disorders (Denicoff et al., 1997). This method has great potential as a diagnostic aid in evaluating the time course and relationship of sleep problems in patients who present with complex sleep, mental, and medical disorders.

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CHAPTER 15

Sexual Dysfunctions and Paraphilic Disorders

LORI A. BROTTO, CAROLIN KLEIN, and KENNETH J. ZUCKER

The sexual and gender identity disorders are classified in separate chapters of the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (*DSM-5*; American Psychiatric Association [APA], 2013). This represents a change from the *DSM-IV-TR* (APA, 2000) in which the (1) sexual dysfunctions, (2) paraphilias, and (3) gender identity disorders were housed within the same chapter. This chapter focuses on sexual dysfunctions, which characterize sexual problems related to the sexual response cycle or pain as well as the paraphilias, which are recurrent, sexually arousing fantasies, urges, or behaviors involving nonconventional or nonconsenting persons and/or objects. Gender identity disorder, renamed gender dysphoria in the *DSM-5*, is covered in a separate chapter.

PART I: SEXUAL DYSFUNCTIONS DESCRIPTION OF SEXUAL DISORDERS

More than 15 years have passed since the approval and subsequent widespread availability of the oral treatments for male sexual dysfunction (e.g., sildenafil, vardenafil, and tadalafil); as a result, research exploring the pathophysiology, epidemiology, assessment, and treatment of sexual dysfunctions has had an unprecedented surge. Methodological sophistication has soared, particularly in the area of neural imaging for low desire and genetic studies of orgasmic dysfunction and dyspareunia. With the publication of the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*; APA, 2013) and the upcoming 11th edition of the *International Classification of Diseases* (*ICD-11*) (forthcoming), there has also been an intensified examination of the reliability and validity of these categories of sexual disorders.

Unlike their division in the *DSM-IV-TR* (APA, 2000), which categorized the sexual dysfunctions according to which phase of Masters and Johnson's four-stage human sexual response cycle (Masters & Johnson, 1966) was disrupted, the *DSM-5* has abandoned this model of linear sexual response. This change was the result of long-standing dissatisfaction with its ability to account for the variability in sexual

response across individuals. In brief, the sexual dysfunctions in previous editions of the *DSM* were separated into disorders of desire, arousal, and orgasm (and pain), which fit with Masters and Johnson's linear conceptualization of the human sexual response cycle—that is, in linear stages from sexual desire to arousal to orgasm. As has been noted (e.g., Binik, 2005, 2010a, 2010b), the sexual pain disorders were added as a fourth category of sexual dysfunction although "pain" was not considered to be part of the human sexual response cycle. This four-category system of diagnosing sexual dysfunctions has been commonplace since *DSM-III* in 1980. However, given numerous criticisms about this linear response cycle, particularly when conceptualizing women's sexual problems, over the past decade there have been concerted efforts to redefine these categories. In particular, concerns about the lack of generalizability of the sexual response cycle for women were that (a) it is based on the sexual response patterns of men; (b) it assumes a linear progression of sexual experience from desire to arousal to orgasm, although healthy sexual experiences can progress in any order and do not need to proceed in this sequence for satisfaction to occur; (c) many of the experiences that are considered normal parts of female sexual response (e.g., fantasizing) are not reported in all women; and (d) characteristics of the sample on which the human sexual response cycle were based are considered biased (Hill & Preston, 1996; Klusmann, 2002; Regan & Berscheid, 1996). One of the alternative classifications that were proposed emerged from an international group of academic clinicians in sexual medicine who were sponsored by the American Foundation for Urologic Diseases to form a consensus panel (Basson et al., 2003). Interestingly, despite the group's criticism about the *DSM-IV-TR* categories of sexual dysfunction, they retained the overall structure and made minor revisions to the diagnostic criteria of the disorders without any attempt made to overhaul the existing nosology.

Another system for classifying sexual dysfunctions as "problems" was proposed by the New View Task Force, led by sexologist Leonore Tiefer. The resulting "New View Document" (Kaschak & Tiefer, 2002; Tiefer, 2001) was a radical departure from the *DSM* classification system and suggested that sexual problems in women have been overdiagnosed and medicalized, and the designating of "dysfunctions" was found to be highly problematic. This alternate system focused on causes instead of symptoms and concluded that such difficulties can be a result of sociocultural, political, or economic factors; partner and relationship status; psychological factors; or medical factors. The New View nosology fervently rejected the biological emphasis of sexual complaints that was inherent in the *DSM*, and the associated "medicalization of sex" that resulted. Empirical support for the New View system is sparse; however, some data suggest the usefulness of this classification scheme in that 98% of the sexual issues in one sample of British women could be classified using the New View framework (Nicholls, 2008).

In the absence of a universally agreed upon underlying model of sexual response, the sexual dysfunctions in *DSM-5* are listed in alphabetical order. This represents a radical departure from past *DSMs* and has generated some controversy (Balon & Clayton, 2014). Collectively, sexual dysfunctions are defined by the *DSM-5* as "a heterogeneous group of disorders that are typically characterized by a clinically significant disturbance in a person's ability to respond sexually or to experience sexual pleasure" (APA, 2013, p. 497). The definition also emphasizes the need for the clinician to exercise clinical judgment when deciding if the difficulty is due to lack of

adequate sexual stimulation, in which case a diagnosis of a mental illness is clearly not appropriate.

The *DSM-5* (APA, 2013) list of sexual dysfunctions includes: delayed ejaculation, erectile disorder, female orgasmic disorder, female sexual interest/arousal disorder, genito-pelvic pain/penetration disorder, male hypoactive sexual desire disorder, premature (early) ejaculation, substance/medication-induced sexual dysfunction, other specified sexual dysfunction, and unspecified sexual dysfunction. Like previous editions of the *DSM,* each sexual dysfunction in the *DSM-5* can be specified as being either lifelong (i.e., the problem has existed since the individual first became sexually active) or acquired (i.e., the problem is new in onset); and generalized (i.e., the problem is not limited to certain types of stimulation, situations, or partners) or situational (i.e., the problem occurs only with select types of stimulation, situations, or partners). The *DSM-5* also has a new severity specifier in which the clinician is asked to rate the level of distress as either mild, moderate, or severe.

Also new to *DSM-5* is a list of five associated features that the clinician should be mindful of during assessment. These are features that may play a role in etiology and/or maintenance of the sexual difficulty and include: (1) partner factors (e.g., a partner's sexual dysfunction), (2) relationship factors (e.g., problematic communication patterns), (3) individual vulnerability factors (e.g., depression or other associated psychopathology), (4) cultural/religious factors (e.g., attitudinal prohibitions against sex), (5) medical factors (e.g., chronic pain or fatigue). During assessment, the clinician is asked to assess each of these domains, taking into account the extent to which each may account for the current presenting complaint. These issues then may be addressed in the course of managing the sexual difficulty.

Whereas criterion A for each of the sexual dysfunctions outlines the diagnostic criteria, criterion B for each delineates the duration criterion in that symptoms must be present for a minimum duration of at least 6 months. The addition of this criterion to *DSM-5* is intended to reduce the probability that temporary or otherwise adaptive changes in sexual functioning may be diagnosed as a sexual dysfunction. Also required for a diagnosis across the sexual dysfunctions is the presence of clinically significant distress in the individual (criterion C).

The range of factors that would exclude the diagnosis of a sexual dysfunction has also been expanded from previous editions of the *DSM.* For example, in addition to the rule-outs due to the presence of another psychiatric disorder, a medication, or a medical condition that completely accounts for the presenting sexual problems, a diagnosis of sexual dysfunction is not made if the symptoms are the result of severe relationship distress (such as domestic violence) or significant stressors.

CLINICAL PICTURE

Delayed Ejaculation Previously known as "Male Orgasmic Disorder," delayed or retarded ejaculation is defined as either a marked delay in ejaculation or the marked infrequency or absence of ejaculation. The difficulty must occur on the majority (approximately 75% or more) of partnered sexual encounters, and take place without the man desiring the delay. Importantly, the symptoms must not be the result of inadequate sexual stimulation. Because the delay leads to extended sexual activity,

some have suggested that it provides a prolonged period of penetration, thus enhancing a female partner's potential for pleasure. Although this may be true, delayed ejaculation is associated with significant distress in both the man and his partner. In some instances, partners may report feeling less attractive due to their partner's inability to ejaculate.

Erectile Disorder

Erectile Disorder (ED) was previously classified as an "Arousal Disorder" in the *DSM-IV-TR*. ED has been the topic of considerable research and academic interest for many decades, but particularly since the approval of the oral phosphodiesterase type 5 inhibitors sildenafil, tadalafil, and vardenafil have been approved and readily available. ED is defined by the *DSM-5* as the presence of at least one of the three following symptoms: (1) marked difficulty in obtaining an erection during sexual activity; (2) marked difficulty in maintaining an erection until the completion of sexual activity; or (3) marked decrease in erectile rigidity. Despite the view among some researchers that erectile difficulties warrant the diagnosis of dysfunction regardless of whether the man is distressed or not, the *DSM-5* requires the presence of clinically significant distress in the individual. Often associated with ED is behavioral avoidance of sexual activities, alterations in self-confidence or mood, and marked anxiety over future sexual encounters.

Female Orgasmic Disorder The study of women's orgasms originated with Freud, who described clitoral orgasms as immature and vaginal orgasms as sexually mature—a theory that has now been discarded. The *DSM-5* defines female orgasmic disorder (FOD) as the presence of either (1) marked delay in, marked infrequency of, or absence altogether of orgasm, or (2) markedly reduced intensity of orgasmic sensations. Since women show wide variability in the factors and types of stimulation that elicit orgasm, the clinician must exercise judgment in determining if the difficulty connotes a sexual dysfunction. Women who are able to reach orgasm via clitoral stimulation only and not through vaginal penetration should not be diagnosed as having FOD.

Female Sexual Interest/Arousal Disorder The diagnosis of sexual interest/arousal disorder (SIAD) is new to *DSM-5* and represents an expansion of the previous diagnosis of hypoactive sexual desire disorder in women. Low sexual desire in women has been the focus of intense research and media attention given the promising findings of pharmaceutical agents for women's complaints of absent desire. However, the lack of approval for any of these medications, and the finding that low sexual desire in women is both highly prevalent and usually multifactorial, suggests that this diagnosis may be especially difficult to treat. Among a number of other reasons, the finding that sexual desire and arousal overlap significantly in women (Brotto, 2010a; Graham, 2010) led to the expansion of the previous diagnosis of low desire, and the deletion of female sexual arousal disorder from the *DSM-5*.

A major change in this diagnosis from previous editions of the *DSM* is the introduction of a polythetic diagnosis in which a woman may experience any three of six possible symptoms in order to meet diagnostic criteria. In brief, these six criteria include: (1) absent or reduced interest in sex, (2) absent or reduced erotic thoughts or

fantasies, (3) difficulties with initiation of sexual activity and receptivity to sex, (4) lack of sexual excitement/pleasure during sex, (5) lack of sexual interest/arousal in response to any sexual triggers (e.g., erotica), and (6) lack of genital or nongenital sensations during sex. The use of polythetic criteria means that two women can have different symptom profiles and still both meet diagnostic criteria for SIAD. Although this has been criticized by some researchers, this also reflects the wide variability across women in the ways their sexual desire is expressed, and the finding that women do not adhere to a single model of sexual excitement (Sand & Fisher, 2007). Since the diagnosis of female sexual arousal disorder was deleted from the *DSM-5,* it is important for clinicians to note that the mere presence of inadequate vaginal lubrication is not grounds for a sexual dysfunction diagnosis, despite the fact that vulvovaginal atrophy is a common problem and often the focus of gynecological care.

Genito-Pelvic Pain/Penetration Disorder

Binik (2005, 2010a, 2010b) has provided compelling arguments for moving the sexual pain disorders from the Sexual Dysfunctions section of the *DSM* to the Pain Disorders category. In summary, the reasoning is that dyspareunia (previously defined as pain with sex in the *DSM-IV-TR*) shares many more similarities to other pain disorders than it does with other sexual dysfunction. However, this proposal was rejected for *DSM-5*, and pain with sexual activity remained as a sexual dysfunction. Nonetheless, this category did undergo a major revision in that the previous diagnoses of dyspareunia and vaginismus (the latter previously defined by significant tension of the pelvic floor muscles, not due to a structural/physical abnormality, which prevents penetration of the vagina) were merged into a single diagnosis newly titled "genito-pelvic pain/penetration disorder" (GPPPD). Furthermore, sexual pain in men was deleted from the *DSM-5* due to insufficient data.

GPPPD is diagnosed when a woman experiences persistent or recurrent difficulties in any one of the following four areas for a minimum duration of 6 months: (1) having vaginal penetration, (2) marked pain with attempted or actual penetration, (3) marked fear or anxiety about vaginal pain, or (4) marked tensing of the pelvic floor muscles during attempted penetration. In some women, the symptoms may lead to extreme avoidance of any attempt at vaginal penetration, whereas in other women, sexual activity may continue despite the presence of symptoms or pain. To adequately assess the fourth criterion of pelvic floor hypertonicity, the assessment must be conducted by a skilled pelvic floor physiotherapist or a gynecologist with expertise in vulvovaginal disorders. Since there are no valid physiological measures of these symptoms, the diagnosis is made entirely based on the woman's self-report.

Male Hypoactive Sexual Desire Disorder A proposal to extend the diagnostic criteria for sexual interest/arousal disorder to men (Brotto, 2010b) was rejected on the grounds of insufficient evidence. Thus, disorders of sexual desire are separated by gender in the *DSM-5*, with most of the previous diagnostic criteria for hypoactive sexual desire disorder (HSDD) being retained in the diagnosis of male HSDD. Thus, a man may meet criteria for male HSDD if he experiences deficient or absent sexual thoughts/fantasies and deficient or absent desire for sex, as long as the symptoms occur for a minimum of 6 months and produce clinically significant distress. Instances of desire

discrepancy in a couple, whereby the man experiences significantly lower levels of sexual desire compared to his partner, are not always indicative of a problem in that individual. Thus, clinical judgment that takes into account age, relationship duration, and other contextual factors must be exercised when making this diagnosis.

Premature (Early) Ejaculation The *DSM-5* defines premature (early) ejaculation (PE), as a persistent or recurrent pattern of ejaculation occurring less than 1 minute following the onset of vaginal penetration, and occurs despite the man's wish. Considerable research has led to the 1-minute criterion, and this definition is also accepted internationally by other sexual medicine societies. The *DSM-5* notes that although ejaculation may occur earlier than desired during other, nonintercourse sexual activities, precise duration criteria have not been established. Reports of lack of control over the impending ejaculation, and associated anxiety are commonplace among men with this disorder. PE has an impact on the man's partner, given that the defining criterion is that ejaculation takes place before, on, or shortly after penetration *with a partner*. In fact, men with PE report fulfilling a partner's needs as being very important to their own rating of sexual satisfaction (Rowland et al., 2004), and Symonds et al. (Symonds, Roblin, Hart, & Althof, 2003) found that 50% of men reported distressing effects of their PE on either finding new relationships or on not satisfying a current partner.

SUBSTANCE/MEDICATION-INDUCED SEXUAL DYSFUNCTION

For instances in which the sexual symptoms are attributable to the effects of a substance (e.g., alcohol) or medication (e.g., selective serotonin reuptake inhibitors), a diagnosis of sexual dysfunction is not made. However, when there is evidence of both (1) sexual difficulties developing during or soon after substance intoxication or medication withdrawal, and (2) knowledge that the given substance or medication is capable of producing sexual symptoms, then a diagnosis of Substance/Medication-Induced Sexual Dysfunction is made. The sexual difficulties must not be due to a separate sexual dysfunction that is not associated with a substance or medication, and must not take place during a state of delirium.

OTHER SPECIFIED SEXUAL DYSFUNCTION AND UNSPECIFIED SEXUAL DYSFUNCTION

The categories of Other Specified Sexual Dysfunction and Unspecified Sexual Dysfunction have replaced the previous *DSM-IV-TR* category of Sexual Dysfunction Not Otherwise Specified. In the case of "other specified," this diagnosis is made when there are symptoms characteristic of a sexual dysfunction and that cause significant distress; however, the symptoms do not meet full criteria for a sexual dysfunction. This category is used when the clinician wishes to indicate the specific reason that the symptoms do not meet full criteria for a disorder. For example, symptoms of sexual aversion or persistent genital arousal might be considered as an Other Specified Sexual Dysfunction. The diagnosis of Unspecified Sexual Dysfunction is reserved for instances in which the clinician chooses not to indicate the reason that the criteria are not met for a specific sexual dysfunction or when there is insufficient information to allow the clinician to make a diagnosis.

DIAGNOSTIC CONSIDERATIONS

Primary care providers are often the first point of contact for individuals with sexual concerns. Adequate assessment requires a thorough biopsychosocial approach, including attention to early family history, relationship and sexual history, and psychiatric status and history, and may require the assistance of a sexual health expert. In some cases, preexisting and confounding contributors may be directly responsible for the sexual issues. For example, relationship factors can mask as sexual dysfunction, as these constructs are highly correlated (e.g., Dennerstein, Lehert, Guthrie, & Burger, 2007). Problems in the relationship can directly impact sexual functioning, and difficulties expressing one's sexual needs can negatively impact sexual desire. In general, men have more difficulty than women with discussing emotional and sexual issues (Banmen & Vogel, 1985). It is important to note that some decline in sexual function is normative with age and relationship duration (Klusmann, 2002) and should not be considered a sexual dysfunction. Cases in which lack of adequate sexual stimulation accounts for the sexual problems should not be diagnosed as a dysfunction. The clinician is advised to take into account factors that affect sexual function, such as age, novelty of the sexual partner or situation, and recent frequency of sexual activity, before making a sexual diagnosis.

Sometimes a sexual difficulty may be an adaptive reaction to a stressful or aversive situation. For example, in homosexuals who are ashamed or insecure about their sexual orientation and who are, thus, in heterosexual relationships, sexual desire may be low in response to individuals of the opposite sex but may be satisfactory toward individuals of the desired sex (Sandfort & de Keizer, 2001). In this case, a diagnosis of sexual desire disorder would not be warranted. The list of associated features for each sexual dysfunction allows a clinician to determine whether individual vulnerability factors, including stress, are contributing to the sexual complaints. This would orient treatment to the stressor and may reduce the likelihood of prematurely resorting to pharmacological aids.

EPIDEMIOLOGY

In the past decade, there have been several international surveys aimed at determining the prevalence of sexual difficulties. The National Health and Social Life Survey (NHSLS), a population-based study of 3,159 American men and women between the ages of 18 and 59 (Laumann, Gagnon, Michael, & Michaels, 1994), had an excellent response rate (79%) and used a combination of face-to-face interviews and questionnaires. The authors inquired about (a) lack of sexual desire, (b) arousal difficulties, (c) problems achieving climax or ejaculation, (d) anxiety about sexual performance, (e) climaxing or ejaculating too quickly, (f) pain during intercourse, and (g) not finding sex pleasurable. The NHSLS found a total prevalence for sexual difficulties of 43% in women and 31% in men (Laumann, Paik, & Rosen, 1999), although these figures may be inflated because the study did not inquire about distress arising from sexual complaints.

The specific prevalence rates for each sexual difficulty in men and women are presented in Tables 15.1 and 15.2, respectively. Of note, these studies of prevalence took place before the *DSM-5* categories were established, so the symptoms are listed in

Table 15.1
Prevalence (%) of Sexual Difficulties According to Age in Men Aged 18–59 (n = 1,249) in the National Health and Social Life Survey (Laumann et al., 1999)

	Age			
Sexual Difficulty	18–29	30–39	40–49	50–59
Lack of interest in sex	14	13	15	17
Unable to achieve orgasm	7	7	9	9
Climax too early	30	32	28	31
Sex not pleasurable	10	8	9	6
Anxious about performance	19	17	19	14
Trouble maintaining or achieving an erection	7	9	11	18

Table 15.2
Prevalence (%) of Sexual Difficulties According to Age in Women Aged 18–59 (n = 1,486) in the National Health and Social Life Survey (Laumann et al., 1999).

	Age			
Sexual Difficulty	18–29	30–39	40–49	50–59
Lack of interest in sex	32	32	30	27
Unable to achieve orgasm	26	28	22	23
Exerienced pain during sex	21	15	13	8
Sex not pleasurable	27	24	17	17
Anxious about performance	16	11	11	6
Trouble lubricating	19	18	21	27

line with the *DSM-IV-TR* (or earlier) categories. Being married and having a higher educational level were each associated with significantly lower rates of sexual difficulties in men and women. Differences according to ethnic status were more prominent for women than for men, with African American women reporting lower levels of sexual desire and pleasure than Caucasian women, but Caucasian women reporting more sexual pain than African American women. In contrast, both groups had higher rates of sexual difficulty than Hispanic women. Emotional or stress-related problems were strongly associated with sexual difficulties, whereas physical health-related problems were more predictive of sexual dysfunction in men only. A decline in social status was related to an increased risk for all types of sexual difficulty for women but only with erectile disorder in men. Quality of life significantly predicted sexual difficulties, particularly for women (Laumann et al., 1999).

Another epidemiological survey assessed 1,335 women and 1,475 men aged 18 to 74 who lived in Sweden (Fugl-Meyer & Sjogren Fugl-Meyer, 1999), and a third study assessed 13,882 women and 13,618 men from 29 countries (Global Study of Sexual Attitudes and Behaviors [GSSAB; Laumann et al., 2005]), with the latter collecting information on the prevalence of sexual concerns in men and women aged 40 to 80, as

well as additional important information on correlates of sexual difficulties. Data from each of these studies are discussed according to the specific sexual symptom assessed and not according to the *DSM-5* diagnosis.

Based on the findings from the NHSLS, low desire occurs in approximately 15% of American men and 30% of American women aged 19 to 59 (Laumann et al., 1999). These numbers are in line with those of the Swedish study, which found the prevalence of low sexual desire to be approximately 16% in men and between 27% and 34% in women (Fugl-Meyer & Sjogren Fugl-Meyer, 1999). Men aged 66 to 74 reported the highest prevalence of low desire at 41% (Fugl-Meyer & Sjogren Fugl-Meyer, 1999). The GSSAB found a very high prevalence of HSDD in women aged 40 to 80 from the Middle East and Southeast Asia (43%; Laumann et al., 2005), whereas the prevalence in men was found to be approximately 22% to 28%. Among women seeking routine gynecologic care, the rate of low sexual interest has been found to be even higher, at 87% (Nusbaum, Gamble, Skinner, & Heiman, 2000); however, when including distress in the diagnosis, the prevalence of low desire in women may drop to less than 10% (Bancroft, Loftus, & Long, 2003).

According to the NHSLS, the prevalence of ED is 7% in men aged 18 to 29 and 18% in men aged 50 to 59 (Laumann et al., 1999). Difficulties in attaining an erection are age associated, with a prevalence of 24% being found in men aged 66 to 74 (Fugl-Meyer & Sjogren Fugl-Meyer, 1999), and a prevalence of 58% being found in men aged 75 to 79 (Monga, Bettencourt, & Barrett-Connor, 2002). Outpatient settings reveal much higher rates of ED. For example, of 1,352 Polish men seeking routine care in an outpatient setting, 43% met criteria for ED (Haczynski et al., 2006). There are also cross-cultural differences in ED prevalence, as shown in the GSSAB study, where there was double the rate in East (27.1%) and Southeast (28.1%) Asia compared to Western countries (Laumann et al., 2005).

Using the *DSM-IV-TR* definition of female sexual arousal disorder, which focused on insufficient lubrication-swelling, prevalence rates range from 10.9% to 31.2% (Laumann et al., 1999; Mercer et al., 2003; Oberg, Fugl-Meyer, & Fugl-Meyer, 2004; Witting et al., 2008), with higher rates once again being found in Southeast (34.2%) and East (37.9%) Asia (Laumann et al., 2005). Bancroft and colleagues (2003) defined low arousal somewhat differently (i.e., decreased sexual arousal during sexual activity, decreased genital tingling, and decreased enjoyment of genital touch) and found this affected 12.2% of women. The only other study to assess the prevalence of subjective sexual arousal difficulties found a prevalence of 17% (Dunn, Croft, & Hackett, 1998). It is notable that the latter subjective arousal impairments are more commonly the presenting complaint in sex therapy clinics, whereas difficulties with lubrication are more likely to present at gynecologic offices or that of the primary care provider.

Premature (early) ejaculation affects approximately 30% of men aged 18 to 59 (Laumann et al., 1999) and is, therefore, considered the most prevalent male sexual dysfunction. This prevalence is relatively uniform around the world, except in the Middle East, where rates are much lower at approximately 12.4% (Laumann et al., 2005); however, controversy in what defines "too early" has led to differing prevalence rates, as the national probability study in Sweden found a prevalence of only 9% (Fugl-Meyer & Sjogren Fugl-Meyer, 1999).

Delayed ejaculation is much less prevalent than premature or early ejaculation, with its prevalence ranging from 2% to 8% (Fugl-Meyer & Sjogren Fugl-Meyer, 1999;

Laumann et al., 1999). Among older men, the prevalence ranges between 9.1% (Northern Europe) and 21.1% (Southeast Asia; Laumann et al., 2005).

The prevalence of female orgasmic disorder in Swedish and American probability samples ranges between 22% and 25% (Fugl-Meyer & Sjogren Fugl-Meyer, 1999; Laumann et al., 1999), with the highest prevalence in the youngest age cohort, perhaps due to a lack of sexual skill and high partner turnover. Rates of anorgasmia are also culturally determined, with the highest prevalence of FOD (41.2%) being in women from Southeast Asia (Laumann et al., 2005).

Pain elicited from sexual activity affects approximately 14% of American women (Laumann et al., 1999) and 30% of East Asian and Southeast Asian women (Lauman et al., 2005), and is one of the most common sexual complaints expressed during routine gynecologic examinations (72%; Nusbaum et al., 2000). Among sexually active adolescent women, the prevalence of pain with intercourse is 20% (Landry & Bergeron, 2009). The prevalence of vaginismus ranges from 1% to 6% of women based on a large review (Weijmar Schultz & Van de Wiel, 2005).

Across epidemiological studies, there are methodological concerns that raise doubt about the accuracy of these figures and concerns about the potential for the medicalization of sexuality (Tiefer, 2002). In part, this debate has been centered on the notion that a sexual difficulty is not necessarily a dysfunction if such a large proportion of the population experiences it. Thus, Bancroft and colleagues (2003) assessed the extent to which sexual difficulties were associated with distress about the sexual relationship and distress about one's own sexuality. They suggested that 24% of the sample experienced a sexual problem that evoked distress (almost half that reported by the NHSLS), and that the findings from the NHSLS are likely inflated. Furthermore, other researchers note that the positive relationship between low desire and age disappears when distress is taken into account (Hayes, Dennerstein, Bennett, & Fairley, 2008). Finally, several studies have found a high prevalence of sexual satisfaction despite the presence of sexual symptoms (i.e., low desire, problematic arousal; Cain et al., 2003).

PSYCHOLOGICAL AND BIOLOGICAL ASSESSMENT

A thorough biopsychosocial interview is considered foundational in the assessment of sexual difficulties. An important aspect in assessing sexual dysfunction is determining whether the problem is related to a psychological versus a biological/organic etiology or both. It is also important for the clinician to distinguish lifelong (primary) versus acquired (secondary) and generalized versus situational difficulties as these may point to important etiological factors. For example, clinicians should inquire about morning erections to gain a sense of the degree to which ED is situational or generalized. Complete loss of morning erections suggests a vascular or neurological component to the ED, and a referral to a qualified urologist is indicated.

Assessment involves face-to-face interviews of the presenting person, ideally together with and separately from the partner, covering known and supposed predisposing, precipitating, and perpetuating issues relevant to the sexual difficulty. These include assessments of mood and general psychiatric status, medications and medical comorbidities, psychosexual history, and personal history. Although many self-report questionnaires are available, none can replace a thorough clinical interview (Brotto, Bitzer, Laan, Leiblum, & Luria, 2010).

Accurate assessment of medical factors often requires physical and laboratory examinations. In men, testosterone that is free, bound to albumin, and bound to SHBG should be measured first thing in the morning. A thorough assessment of sexual interest/arousal disorder in women involves separately assessing for difficulties in mental sexual arousal and interest versus genital excitement. Assessment of GPPPD may include a physical examination of the level of voluntary control of the pelvic floor muscles, pelvic floor muscle tonus, presence of vaginal wall prolapse, signs of vaginal atrophy, size of introitus, presence of discharge, evidence of infection (acute or chronic), epithelial disorders, and/or pain by a qualified health professional (usually a gynecologist or primary care provider with specialized training in vulvovaginal disorders).

To assess for the criterion of marked vulvovaginal pain when making a diagnosis of GPPPD, the physician often uses the cotton swab test in which the vestibule is palpated with a cotton swab and the woman reports areas of particular tenderness or pain. In addition to pain and tenderness upon touch, there is erythema (redness) in the area of the vestibule (Friedrich, 1987). During such an assessment, it is important for the clinician to elicit as much information as possible regarding the qualities of pain (location, intensity, characteristics). Because the elicitation of pain may evoke distressing emotions for the woman, it is important for the clinician to be sensitive to the woman's emotional state and only conduct the genital exam if sufficient explanation and preparation has been given. Since pelvic floor muscle spasms have been found to be an unreliable indicator of GPPPD, the diagnosis is largely based on the patient's self-report of difficulties with intercourse, including anticipation of pain, anxiety, and phobic avoidance.

Assessment of PE in clinical trials has adopted the stop-watch technique in which the duration of time between penetration and ejaculation is monitored, usually by the man's partner. Studies using this methodology have led to the current recommendation that one minute be used as the threshold for determining when early ejaculation might constitute a sexual dysfunction. However, this additional layer of performance anxiety may artificially inflate the man's dysfunction, leaving this technique suboptimal, particularly when making a diagnosis of PE. Accurate assessment can also be confounded by embarrassment (Symonds et al., 2003). Grenier and Byers (2001) found marked differences in the prevalence of PE depending on the operational definition of "rapid." They concluded that a multifaceted approach should include assessment of behavior, affect, self-efficacy, and the degree of severity of different dimensions of PE.

ETIOLOGICAL CONSIDERATIONS

As implied in the previous section on assessment, all the sexual dysfunctions are considered to be biopsychosocial in their etiology. Although previous editions of the *DSM* included the specifier of "due to psychological factors" or "due to combined factors," this has been eliminated from the *DSM-5* due to the recognition that this level of delineation is rarely possible. Even in cases when there is a clear biological or medical etiology to the sexual symptoms, sexual functioning typically involves an integration of all organ systems of the body, the vascular system, muscles, and the brain, making multifactorial etiology the norm rather than the exception.

Low desire in both men and women is considered to result from a combination of organic and psychological factors. In women, relationship duration, age, feelings for one's partner, and depression have all been associated with sexual desire disorder (Brotto et al., 2010). In fact, 27% to 62% of women with low desire also meet criteria for a depressive disorder (Hartmann, Heiser, Ruffer-Hesse, & Kloth, 2002; Phillips & Slaughter, 2000). Interestingly, a few studies report that depressed mood is associated with increased frequency of masturbation (Cyranowski et al., 2004; Frolich & Meston, 2002)—one potential index of sexual desire. Low testosterone and testosterone metabolites have not been found to significantly differentiate women with and without HSDD, although the latter are found to have lower levels of the androgen precursor, dihydroepiandrosterone (DHEA; Basson, Brotto, Petkau, & Labrie, 2010). Women with HSDD show different patterns of neural activation particularly in neural circuits involved with encoding arousing stimuli, retrieval of past erotic situations, or both (Arnow et al., 2009).

Recent studies on cultural influences in low desire have shown women from East Asian heritage to have lower levels of desire compared to women from European descent. Moreover, among the East Asian women, those with higher levels of mainstream (i.e., Westernized) acculturation had higher sexual desire than those who retained their culture or heritage (Woo, Brotto, & Gorzalka, 2011). The variable "sex guilt," or "a generalized expectancy for self-mediated punishment for violating or for anticipating violating standards of proper sexual conduct," has been shown to mediate the relationship between culture and sexual desire in women. Therefore, sex guilt may be a future treatment target among ethnic minority women presenting with sexual desire complaints (Woo et al., 2011).

Androgen deprivation and hyperprolactinemia seem to play a more pertinent role in HSDD in men (Brotto, 2010b). Hyperprolactinemia may result from antipsychotic medications or prolactin-secreting tumors. With respect to androgen deprivation, as men age, sex hormone binding globulin (SHBG) levels increase, thereby decreasing the level of free testosterone. Similarly, bioavailable testosterone begins to decline when men are in their 30s and 40s, and continues to decline throughout the life span (Seidman, 2003). A syndrome known as androgen deficiency in the aging male (ADAM) or partial ADAM (PADAM) can include fatigue, depression, reduced sex drive, erectile disorder, and changes in mood and cognition (Morales, Heaton, & Carson, 2000). There is significant comorbidity between ED and HSDD in men such that men experiencing erectile difficulties eventually have reduced levels of desire.

In men, hypothyroidism, hypogonadism, and hyperprolactinemia are also associated with ED (Morales et al., 2004). Radical genital or pelvic surgeries can result in a sudden loss of erectile function, such as the case with prostate cancer surgery (Bolt, Evans, & Marshall, 1987; Stanford et al., 2000), especially if the procedure did not involve nerve-sparing techniques. Among men treated for diabetes, the prevalence of ED is 28% (Feldman, Goldstein, Hatzichristou, Krane, & McKinlay, 1994). Overall, any medical condition that causes blood vessel damage will likely negatively impact erectile function. Although often presumed to have an exclusive organic etiology, it is suspected that there are many cases of ED where psychological factors are responsible but go unrecognized. For example, major depressive disorder has been strongly associated with ED (Araujo, Durante, Feldman, Goldstein, & McKinley, 1998).

Distinguishing ED that is secondary to the depression itself versus as a result of antidepressant use (Ferguson, 2001) is an important consideration.

Performance anxiety is also strongly associated with erectile dysfunction. Anxiety or stress may activate the sympathetic nervous system, which can both increase smooth muscle tone and interfere with signals from the sacral spinal cord. The man with no prior history of ED who fails to reach an erection one time due to stress or other factors may become concerned about his future erectile ability such that his ED is maintained by performance anxiety. Implicit in this example is the phenomenon that factors that maintain a sexual dysfunction may not be the same factors that initially triggered the complaint.

In the case of women, vaginal photoplethysmography as a measure of genital vagocongestion has not been able to differentiate women with from those without significant sexual arousal concerns (Laan, van Driel, & van Lunsen, 2008). For this reason, it is assumed that impairments in genital blood flow do not underlie genital arousal complaints of women. The reasons for women's lack of awareness of their genital responding, otherwise known as desynchrony (or lack of concordance), compared to men (Chivers, Seto, Lalumiere, Laan, & Grimbos, 2010) has become the focus of study because it may shed light on different models of sexual responding between the sexes.

The precise etiology of PE is unknown, but a combination of psychological, biological, and behavioral components likely contribute. Much of the research exploring etiology in PE is based on rodent studies in which serotonergic disruption is the primary etiological factor. Stimulation of 5-HT_{1A} receptors in rats leads to rapid ejaculation, whereas hyposensitivity at the 5-HT_{2C} receptor shortens ejaculation time (Waldinger, 2002). Studies in rodents have led Waldinger, a leading authority on PE, to formulate the Ejaculation Threshold Hypothesis, which posits that men with PE have a lower ejaculatory setpoint (threshold) due to low serotonin neurotransmission, leading them to tolerate only a very low amount of sexual arousal prior to ejaculation (Waldinger, 2005). There is also evidence of a genetic predisposition to PE given the finding that 71% of first-degree relatives of men with PE also have the condition (Waldinger, Rietschel, Nothen, Hengeveld, & Olivier, 1998).

Acquired and/or situational PE may suggest a more psychological etiology related to early sexual experiences, low frequency of sexual activity, or poor ejaculatory control techniques. Among men with PE, 50% of the female partners meet criteria for anorgasmia and 54% meet criteria for hypoactive sexual desire (Fugl-Meyer & Sjogren Fugl-Meyer, 1999), suggesting a reciprocal relationship between PE and women's sexual complaints. Masters and Johnson (1970) forwarded the possibility that performance anxiety leads to loss of ejaculatory control, but more recent research does not support the role for anxiety in PE in the clinical or the laboratory setting (Strassberg, Kelly, Carroll, & Kircher, 1987). Instead, high anxiety, if present, may be the consequence, rather than the cause, of PE.

Waldinger (2005) has speculated that organic factors related to genetics have a likely role in etiology. In particular, aberrations in the serotonergic system, such as hyperactivity at the 5-HT_{2C} receptor and hypoactivity at the 5-HT_{1A} receptor, have been found in rodent studies to be related to delayed ejaculation. Androgen deficiency with aging and/or hypogonadism is also linked to Delayed Ejaculation, as are age and prostate disease (Laumann et al., 2005). Injury to the lumbar sympathetic ganglia (i.e.,

such as from multiple sclerosis) may also delay ejaculation. One chart review has suggested that idiosyncratic masturbatory style (e.g., using rapid stimulation or pressure in a manner that is not easily duplicated by partnered sexual activity), as well as using a variant sexual fantasy (e.g., fantasy about S&M), act as predisposing factors for delayed ejaculation (Perelman, 2006).

The same organic factors implicated in delayed ejaculation in men have been associated with FOD in women (e.g., neurologic injury, SSRI use, alcohol). There may also be a genetic aspect to orgasmic difficulties in women given the finding of higher correlations between orgasmic frequency during masturbation and orgasmic frequency during sexual intercourse in monozygotic twins compared to dizygotic twins (Dunne et al., 1997). In addition, the heritability for orgasm problems with intercourse is 31% to 34%, and the rate for orgasm problems in masturbation is 37% to 45% (Dunn, Cherkas, & Spector, 2005).

Psychological factors found to be associated with anorgasmia in women include lower educational levels, high religiosity, sex guilt (Laumann et al., 1999), and a dim outlook for the future (Laumann et al., 2005). Although sexual abuse has been associated with anorgasmia in some studies, other studies have failed to find such a relationship. There does not appear to be a correlation between relationship satisfaction and orgasmic ability, given that many women are sexually satisfied with their partners despite not consistently or, perhaps, ever attaining orgasm with intercourse (Basson, 2004).

Pelvic or vulvar surgeries, chemotherapy, or radiation have all been associated with dyspareunia (Amsterdam, Carter, & Krychman, 2006), as have menopausal changes due to loss of estrogen and subsequent loss of elasticity in the vaginal tissues. In one type of genital pain, provoked vestibulodynia (PVD), biological etiological factors have included yeast infections, use of oral contraceptives, early menarche, a genetic predisposition, human papillomavirus, and urethral conditions or infections (Pukall, Payne, Kao, Khalifé, & Binik, 2005; Pukall, Strigo, et al., 2005). Assessment with functional magnetic resonance imaging (fMRI) indicates that women with PVD have a more general hypersensitivity to touch and pain compared to unaffected women (Pukall, Strigo, et al., 2005).

Although psychological factors are not considered primary in GPPPD, personality and psychiatric symptoms can exacerbate pain as well as pain-induced affect. Among the many psychological factors correlated with genital pain are anxiety, depression, low self-esteem, harm avoidance, somatization, shyness, and pain catastrophization (as summarized in Pukall, Payne, et al., 2005).

With regard to the pelvic floor muscle contractions that characterize GPPPD, Weijmar Schultz and Van de Wiel (2005) summarize eight major theories of etiology. Although these researchers focused on the *DSM-IV-TR* category of vaginismus, one could easily apply their findings to GPPPD. One theory is a behavioral view in which a conditioned anxiety reaction results in vaginal muscle spasm. This conditioning may have taken place during one episode of learning (e.g., as in the case of sexual assault with forced penetration) or over repeated trials (e.g., as in the case of voluntary intercourse in a woman with dyspareunia). The fear of pain from intercourse and the subsequent avoidance of any genital contact maintains the phobic anxiety.

According to the overactive pelvic floor muscle view (Weijmar Schultz & van de Wiel, 2005), some have regarded the pelvic floor muscle symptoms of GPPPD as a

pelvic floor dysfunction and not as a sexual dysfunction. Because conditioning is the likely mechanism behind the overactive pelvic floor muscles, physiotherapy with biofeedback is the most logical treatment approach (Rosenbaum, 2003).

The interactional view (Weijmar Schultz & van de Wiel, 2005) suggests that pelvic floor hypertonus maintains balance between partners. Although research on this view is sparse, it is not uncommon in the clinical setting for male partners to be passive, dependent, anxious, and lacking in self-confidence. There is also evidence that these partners suffer from sexual dysfunction themselves (Lamont, 1978); therefore, GPPPD may function to maintain balance in the sexless relationship.

COURSE, PROGNOSIS, AND TREATMENT

As implied in the section on etiology, there has been a pendulum shift in the past decade and a half, with much research attention focused on finding effective pharmacological treatments for the most prevalent sexual complaints (low desire in women, erectile and ejaculation difficulties in men). As a result, there has been a recent dearth of randomized controlled trials of psychological treatments, and much of the information on efficacy of psychological treatments is based on studies conducted in the 1970s and 1980s. However, psychological treatments are effective and needed (Heiman, 2002).

Treatment for HSDD largely depends on the presumed etiology and can involve any combination of psychotherapy (either alone or with the partner), medications, or hormonal therapy. Psychological therapy may involve exploration of couple issues, including anger, trust, exploration of an affair, and feelings of attractiveness. Treatment may also encourage the use of fantasies, erotic stimuli, and other forms of sexual activity besides intercourse. Unfortunately, there are no controlled publications on the efficacy of psychological treatment without concomitant medication treatment for HSDD in men.

Among the pharmacological treatments for low desire, bupropion (marketed as the antidepressant Wellbutrin) is a norepinephrine and dopamine agonist that has been found to have an efficacy rate of approximately 86% in nondepressed men with HSDD (Crenshaw, Goldberg, & Stern, 1987). Testosterone replacement has been the primary hormonal treatment studied for men with HSDD and is administered as an injection, a patch, or a gel. In a recent meta-analysis of the effects of testosterone on sexual dysfunction in men with heterogeneous sexual complaints, testosterone treatment improved sexual desire among men with clinically low levels of testosterone but not in men with normal levels (Isidori et al., 2005).

Treatments have been tested on the previous *DSM-IV-TR* diagnoses of Hypoactive Sexual Desire Disorder and Female Sexual Arousal Disorder, and not on the *DSM-5* condition of SIAD. Much recent attention has been focused on finding an effective dose and method of administration of testosterone for improving women's sexual desire, and several randomized, placebo-controlled trials investigating a transdermal testosterone patch for improving desire in postmenopausal women receiving estrogen replacement have shown a benefit (e.g., Davis et al., 2006; Kroll et al., 2004). Given a concern over the lack of long-term safety data, particularly with the possible link of testosterone and breast cancer (Tworoger et al., 2005), the testosterone patch did not receive regulatory approval by the Food and Drug

Administration (FDA) and, therefore, continues to be prescribed "off-label" until sufficient long-term safety data are accrued. More recently, BioSante's topical testosterone, Libigel, failed to show benefits significantly greater than the placebo group, despite initial optimism by the company (http://seekingalpha.com/news-article/2106668-biosante-pharmaceuticals-announces-results-from-libigel-efficacy-trials).

The failed antidepressant and serotonin-1A receptor agonist/2A antagonist and dopamine-4 receptor partial agonist, flibanserin, had been shown to significantly improve sexual desire among women with HSDD (Clayton, Dennerstein, Pyke, & Sand, 2010). However, it was rejected by the FDA in 2010 due to the relatively minimal benefit beyond placebo and the concern over side effects. Flibanserin continues to be tested in clinical trials at the current time.

The synthetic hormone tibolone, which has estrogenic, androgenic, and progestogenic effects, has been found to significantly increase sexual desire, frequency of sexual fantasies, and sexual arousability in a randomized, double-blind study of postmenopausal women free of sexual complaints (Laan, van Lunsen, & Everaerd, 2001); however, although it is licensed for the treatment of menopausal symptoms in Europe, it does not have FDA approval in the United States.

Much more recently there have been initial promising results from two new agents, Lybrido and Lybridos, for improving sexual desire among women who are considered to be relatively insensitive to cues for sexual desire or to be prone to sexual inhibition. Lybrido is a combination of 0.5 mg testosterone in a cyclodextrin carrier combined with 50 mg sildenafil citrate in a powder-filled gelatin capsule. Among women with low desire due to a relatively insensitive system for sexual cues ($n = 29$), lybrido led to a significantly greater genital arousal response to a sexual fantasy (but not to sexual films), and significantly higher sexual desire and satisfaction during sexual events compared to placebo (Poels et al., 2013). Lybrido had no effect on women with low desire who were highly sensitive to sexual cues. Lybridos, on the other hand, is a combination of 0.5 mg testosterone in a cyclodextrin carrier and 10 mg buspirone in a powder-filled gelatin capsule. Among 28 women who were considered to be "high inhibitors" (i.e., those with high acute serotonergic inhibitory control), treatment significantly increased genital arousal response to a fantasy (but not to sexual films) as well as subjective reports of desire and satisfaction during sex compared to placebo (van Rooij et al., 2013). Lybridos had no effect on women with low desire and who had low inhibitory mechanisms.

Cognitive and behavioral therapies (CBT) for low desire have moderate empirical support. For example, Trudel and colleagues (Trudel et al., 2001) compared the effects of CBT to a wait-list control in 74 couples in which women met criteria for HSDD. Treatment included psychoeducation, skills and emotional training, and couple assignments in a group format. After 12 weeks, 74% of women no longer met diagnostic criteria for HSDD, and this stabilized to 64% after 1-year follow-up. In addition to significantly improved sexual desire, women also reported improved quality of marital life and perception of sexual arousal.

Interestingly, CBT addressing a different aspect of the sexual response cycle—namely, orgasm—is also effective in increasing sexual desire in women (Hurlbert, 1993) and provides additional evidence that components of sexual response are highly correlated. Several studies including both members of the couple, which tested the

efficacy of marital therapy for women's low desire, have also found promising effects on sexual desire (Fish, Busby, & Killian, 1994; MacPhee, Johnson, & Van der Veer, 1995).

Most recently, two uncontrolled trials have found significant beneficial effects of a mindfulness-based CBT for women with mixed desire and arousal difficulties (Brotto, Basson, & Luria, 2008; Brotto et al., 2008). These findings emphasize the importance of mindfully participating in the body and its sensations during sexual activity. Whether such mindfulness-based interventions show benefit above and beyond treatment as usual or a placebo group is currently being investigated.

Focusing on the specific complaint of genital arousal, there have been numerous recent investigations of pharmacologic treatments, particularly for women with genital sexual arousal disorder; however, all remain unregulated for use for this condition. The dopaminergic agonist apomorphine SL was found to significantly improve sexual arousal, desire, orgasm, satisfaction, and enjoyment when taken daily at 2–3 mg doses but not when taken on an as-needed basis (Caruso et al., 2004). Phentolamine mesylate, commonly used to treat ED, significantly improved self-reported lubrication and tingling sensations, but had no effect on physiological sexual arousal, subjective pleasure, or arousal in postmenopausal women when administered orally (Rosen, Phillips, Gendrano, & Ferguson, 1999). In a much larger, double-blind replication of the study, vaginally applied phentolamine significantly increased physiological arousal in postmenopausal women receiving hormone replacement (Rubio-Aurioles et al., 2002).

The remarkable success of the PDE5 inhibitors for men has initiated a race to find efficacious treatments for women's sexual arousal complaints. However, studies using sildenafil have yielded conflicting findings (Basson & Brotto, 2003; Basson, McInnes, Smith, Hodgson, & Koppiker, 2002; Berman, Berman, Toler, Gill, & Haughie, 2003; Caruso, Intelisano, Lupo, & Agnello, 2001), and there are no published investigations of either vardenafil or tadalafil in women specifically with complaints of genital arousal.

Currently, one product has been approved by the FDA for the treatment of Female Sexual Arousal Disorder. The EROS Clitoral Therapy Device (CTD; Urometrics, St. Paul, MN) is a small, hand-held, battery-operated device that is placed over the clitoris and increases blood flow through gentle suction. The EROS-CTD was found to significantly improve all measures of sexual response and satisfaction in women with FSAD (Billups et al., 2001) and in women with arousal complaints secondary to radiation therapy for cervical cancer (Schroder et al., 2005), but lack of a control condition and the fact that women were required to use the device several times per week for the duration of the study makes it difficult to ascertain whether positive effects were due to the suction, per se (in which case a vibrator might suffice), or to nonspecific attentional factors.

Erectile Disorder

With the approval of sildenafil citrate (Viagra, Pfizer Inc.) in the United States in 1998, treatment for ED is vastly different than it was a decade ago. Sildenafil is a phosphodiesterase type-5 (PDE5) inhibitor that has become a first-line treatment for ED. All PDE5 inhibitors work by inhibiting the action of PDE5, a molecule in

the corpus cavernosum of the penis that is involved in detumescence (loss of erection). There are almost 2,000 published studies in various subgroups of men with ED ranging in age from 19 to 87 years. The drug, in 20, 50, or 100 mg doses, is taken 1 hour before planned sexual activity with a low-fat meal and must be combined with subjective or mechanical sexual stimulation. Its effectiveness ranges from 43% for men with radical prostatectomy, to 59% of those with diabetes, and to 84% for men with ED due to psychological causes (Osterloh & Riley, 2002).

Tadalafil (Cialis, Lilly ICOS LLC.) is a newer PDE5 inhibitor with a 17.5-hour half-life, which promotes greater sexual spontaneity—an important factor for some couples. A large analysis of 2,100 men taking tadalafil found that the drug was significantly more effective than placebo among all subgroups of men studied, including those with diabetes, hypertension, cardiovascular disease, hyperlipidemia, depression, and benign prostatic hyperplasia, and across ethnocultural groups (Lewis et al., 2005).

Vardenafil (Levitra, Bayer) is another PDE5 inhibitor that has been found to be particularly effective for two difficult-to-treat groups: namely, men with diabetes and men who have undergone a radical prostatectomy. More than 70% of men in both groups responded to vardenafil with improved erections (Brock et al., 2001; Goldstein, Fischer, Taylor, & Thibonnier, 2002).

Before the approval of the PDE5 inhibitors, injectable and intraurethral treatments were considered the mainstay of ED treatment. Traditionally reserved for men with an organic basis to their ED, these techniques involve intracavernosal injection of alprostadil (prostaglandin E1) directly into the penis, and, unlike the oral medications, sexual stimulation is not necessary for an erection. Although these treatments were found to be highly effective in 87% of men (Linet & Ogrinc, 1996), the side effects of penile pain or prolonged erections make compliance a concern. Alprostadil can also be delivered directly into the urethra as MUSE (medicated urethral system for erection). This mode of delivery is favorable for men who cannot tolerate oral medications or injections. Approximately 70% of men respond positively to MUSE (Padma-Nathan et al., 1997), which requires some training from a sexual health clinician for proper insertion. Testosterone therapy, both alone (Isidori et al., 2005) and in combination with a PDE5 inhibitor (Shabsigh, 2005), has also been found effective in the treatment of erectile disorder.

Vacuum constriction devices (VCD) and constriction rings are also available for ED and do not require administration/ingestion of a medication. A VCD is a cylindrical tube that is placed over the flaccid penis, and a vacuum draws blood into the penis either manually or with a battery-operated motor. A constriction ring is then typically placed over the base of the penis to sustain the erection for intercourse. Although very effective for men who cannot tolerate medical forms of ED treatment, it does require a certain degree of manual dexterity and is not suitable for men with sickle cell disease, leukemia, or those who are using anticoagulation treatments (Wylie & MacInnes, 2005).

Psychological techniques can be essential for couples in which relationship discord and difficulties in communication are related to the ED. However, considerably less research has examined the efficacy of psychological therapies for men with ED, although multiple case reports indicate benefit from combined oral medications plus cognitive behavioral therapies (McCarthy, 1998; Perelman, 2002; Segraves, 1999).

Seman's Squeeze technique is a highly effective behavioral treatment for PE. The method requires the man to provide direct feedback to his partner when he feels an ejaculatory urge. The couple discontinues sexual stimulation, and the partner applies pressure to the glans of the penis until the urge is reduced (Masters & Johnson, 1970; Semans, 1956). The technique can be used during masturbation before attempting it with a partner. The efficacy of the Squeeze technique is approximately 60% (Metz, Pryor, Nesvacil, Abuzzahab, & Koznar, 1997). The Stop-Pause approach is very similar but, because it involves a reduction in penile stimulation as the man nears ejaculatory inevitability, it better simulates natural behaviors during intercourse (Kaplan, 1989). Sexual stimulation is resumed once the man feels control over his ejaculation. Although early studies by Masters and Johnson and Kaplan found efficacy rates nearing 100%, more recent controlled trials find efficacy in the range of 64% (Hawton, Catalan, Martin, & Fagg, 1986). Other behavioral interventions such as self-administered psychological treatment (Trudel & Proulx, 1987) or pelvic floor rehabilitation (Giuseppe & Nicastro, 1996) have been reported successful in uncontrolled trials.

Based on the hypothesis that a low ejaculatory setpoint due to low serotonin neurotransmission may underlie some forms of PE, selective serotonin reuptake inhibitors (SSRIs) have become a mainstay of pharmacological treatment. This SSRI effect takes advantage of one of the negative side effects of SSRI use, namely delayed orgasm in men and women. Several dozen trials examining the efficacy of SSRIs in PE have been conducted, and a recent meta-analysis of daily SSRI use showed paroxetine to have the greatest efficacy in delaying ejaculation (Kara et al., 1996).

Pharmacological treatment for PE may also include topical local anaesthetics applied to the penis. For example, lidocaine and/or prilocaine appear to be effective in about 85% of men (Xin, Choi, Lee, & Choi, 1997). Finally, a comparison of behavior therapy with and without sildenafil shows the combination to significantly delay time to ejaculation (Tang, Ma, Zhao, Liu, & Chen, 2004).

In cases of an organic etiology, amelioration of the underlying biological factors is an important first line of treatment. This may include switching the patient to a different antidepressant, androgen administration, or attempts to control diabetic neuropathy. Kaplan (1974) described a shaping procedure in which a male partner with situational Delayed Ejaculation masturbates in front of his female partner on the other side of the room and subsequently masturbates while moving progressively closer and closer to her, with the goal of eventual ejaculation inside the vagina. No controlled trials exist, but clinical observation supports its efficacy for a large proportion of men. In addition, individual or couple therapy may be warranted if there are perpetuating interpersonal factors.

Female Orgasmic Disorder

Both psychological and pharmacological treatments have been found to be effective for female orgasmic disorder (FOD). Directed masturbation exercises (Masters & Johnson, 1970) are designed to teach women to focus on sexually erotic cues, not focus on distracting nonsexual cues, and apply graded stimulation to the clitoris in an effort to become orgasmic with masturbation. The self-help book *Becoming Orgasmic: A*

Sexual Growth Program for Women recommends these exercises (Heiman & LoPiccolo, 1987) and has an approximate 90% efficacy rate.

Because anxiety may act as a cognitive distraction, thereby distracting the woman away from sexual cues, anxiety reduction is often a target in treatment. Systematic desensitization involves training the woman to relax the muscles of her body while presenting her with sexual anxiety-evoking stimuli. Sensate focus involves having a partner touch the woman, with her verbal guidance, while she focuses on relaxation (Masters & Johnson, 1970). These interventions were efficacious when treatment was administered by a therapist, or in a group or self-help format (Libman et al., 1984).

In the coital alignment technique (CAT), the man is in the superior position and shifts forward such that the base of his penis makes direct contact with the woman's clitoris. This ensures constant clitoral stimulation and results in improved coital orgasmic ability in approximately 56% of women (Hurlbert & Apt, 1995). The EROS-CTD, described earlier for FSAD, has also been found to significantly improve orgasmic ability in women with FOD (Billups et al., 2001).

Several placebo-controlled studies have examined the efficacy of pharmacologic treatments for FOD. For example, pre- and postmenopausal women with low arousal and anorgasmia showed significant improvements with sildenafil (Basson & Brotto, 2003; Caruso et al., 2001). In a double-blind trial of 100 mg sildenafil versus placebo for women with SSRI-induced FOD, there were significantly fewer sexual side effects in the sildenafil group (Nurnberg et al., 2008). However, given the study's highly selective inclusion criteria and the difficulties in recruiting participants to the trial, the generalizability of these findings remains tentative.

Previously empirically tested treatments have focused either on Dyspareunia or Vaginismus (*DSM-IV-TR)* and not on GPPPD. There are four general categories of treatment for provoked vestibulodynia (PVD), a type of GPPPD and the most common cause of dyspareunia: (1) medical, (2) psychological, (3) physical, and (4) surgical. Among the medical treatments for PVD, suggestions include hygiene modification and sitz baths, topical anesthetics or corticosteroids, oral treatments in the form of low-dose antidepressants, anticonvulsants, oral corticosteroids, or antifungals, and injectable treatments. Unfortunately, there is a lack of randomized double-blind and prospective studies assessing these treatments, so precise efficacy rates are not available.

Behavioral treatments such as CBT adopt pain control strategies as their primary target and include Kegel exercises, vaginal dilatation, relaxation, and cognitive challenging (Bergeron & Binik, 1998). Physiotherapy with pelvic floor biofeedback has also been found to be very effective (Bergeron et al., 2002). Surgery, usually in the form of vestibulectomy, involves excision of the hymen and sensitive areas of the vestibule. Recent studies demonstrate a high degree of efficacy (73% to 90%; Gaunt, Good, & Stanhope, 2003; Lavy, Lev-Sagie, Hamani, Zacut, & Ben-Chetrit, 2005); however, results are lower for women with acquired PVD, who also have a higher rate of recurrence (Rettenmaier, Brown, & Micha, 2003). Most recently, there is evidence of a four-session mindfulness-based treatment for improving pain and reducing catastrophizing and pain hypervigilance in women with PVD when treated in group format (Brotto, Basson, Driscoll, Smith, & Sadownik, in press).

In the only published, randomized, head-to-head comparison of 12-week group CBT, pelvic floor physiotherapy, and vestibulectomy, 78 women were followed for a

2-year period (Bergeron et al., 2001). All groups experienced a significant reduction in pain at posttreatment and at 6-month follow-up, with the vestibulectomy group showing the greatest degree of improvement (Bergeron et al., 2001). All groups also significantly improved on measures of psychological and sexual function. A 2.5-year follow-up of the study found continued improvement in all three groups, with no significant treatment differences in pain from intercourse, sexual functioning, or intercourse frequency (Bergeron, Khalife, Glazer, & Binik, 2008).

According to the behavioral view, treatment of vaginismus involves a reconditioning of the body's response to feared objects such as the penis, a speculum, or a tampon, much like the treatment approach for other specific phobias. Using a systematic desensitization approach, the woman is asked to create a hierarchy of feared objects, which she will then progressively work through to insert vaginally over the course of treatment. Simultaneously, the woman is taught to engage in activity incompatible with tension or anxiety, such as relaxation and diaphragmatic breathing. Highly useful as an object of insertion is the vaginal dilator (or insert or accommodator), shown in Figure 15.1 (Laurel Prescriptions, Vancouver, Canada), which can be made of wax, plastic, silicone, or other nonirritating substances. Research examining the efficacy of this behavioral approach combined with cognitive elements found it to be highly effective for nearly all women in reducing vaginismus, anxiety, and improving the couple relationship (Kabakci & Batur, (2003). A prospective study of CBT in women with vaginismus was found to be effective, and benefits were mediated by changes in fear of intercourse and changes in avoidance behavior (ter Kuile et al., 2007).

Figure 15.1 Vaginal dilators (Laurel Prescriptions, Vancouver, Canada) for the treatment of vaginismus. *Source:* © Laurel Prescriptions.

CASE STUDY

Hypoactive Sexual Desire Disorder in a Man

Robert is a 64-year-old married, Caucasian, heterosexual man. He and his wife, Cecile, age 58, have been married for 36 years and have three adult children ages 35, 31, and 28. Robert presented to his primary-care doctor with complaints of "lost libido," which he thought might be due to a "hormonal imbalance." Robert's physician conducted a brief but focused assessment of his loss of desire, focusing on how Robert defined desire, the impact on his self-esteem and relationship, and an exploration of other contributing factors in Robert (and Cecile's) lives. The physician ordered a complete hormone profile, focusing on Robert's levels of bioavailable testosterone. Robert reported that in the past 5 years he became less interested in sex, thought about sex less than once per week (previously he would think about it daily), and only very reluctantly initiated sexual activity. He became quite anxious about sex in the evenings, which was typically when sexual activity would occur. Although Cecile was not present during this appointment, Robert noted that Cecile had also experienced a reduction in sexual interest, and that she had increased vaginal dryness over the past few years coinciding with menopause.

When asked what steps Robert and Cecile have taken on their own to improve Robert's desire for sex, he stated that they were unsure, and this is what prompted their speaking to the physician. Robert noted that there had also been recent problems with his erectile capacity. He was unable to reach an erection in approximately 50% of his sexual attempts. Robert concluded the appointment by stating that these changes were quite distressing to him, and he worried about becoming less attractive to Cecile. Therefore, he was quite motivated for treatment. The physician referred Robert and Cecile to a sex therapist to provide some educational information on normative sexual function changes with age and relationship duration, and to discuss with Robert and Cecile sexual skills (e.g., sensate focus) that might improve the quality of their sexual interactions. The sex therapist could also address Robert's anxiety as well as perform a more thorough assessment of mood and lifestyle factors. Although the physician suggested examining Robert's hormonal profile, he knew that Robert was otherwise "hormonally healthy" and showed no clinical signs of hypogonadism.

SUMMARY OF SEXUAL DYSFUNCTIONS

The past 15 years have seen an unprecedented increase in research aimed at understanding the etiology, pathophysiology, prevalence, diagnostic features of, and treatments for sexual dysfunction. The increased presence of the pharmaceutical industry's interests in this field has led to increased research funding, but this boom has also been associated with caution and criticism for fear of medicalizing conditions that many argue are largely influenced (and created) by sociopolitical and psychological pressures. With the *DSM-5* now published and widely available, it is incumbent upon the field of sex therapy and research to generate new data as to the pathophysiology, assessment, and treatment of the current roster of sexual dysfunctions.

PART II: PARAPHILIC DISORDER

Description of Paraphilias

The paraphilias, as defined in the *DSM-5* (APA, 2013), refer to "any intense and persistent sexual interest other than sexual interest in genital stimulation or preparatory fondling with phenotypically normal, physically mature, consenting human partners" (p. 685). The paraphilias cluster into two main types: The first involves anomalous activity preferences (courtship disorders, which resemble distorted components of human courtship behavior, or algolagnic disorders, which involve pain and suffering); the second involves anomalous target preferences, which are either directed at other humans or elsewhere.

The term *paraphilia* was coined by Stekel in 1923 and translates into love (*philia*) beyond the usual (*para*) (Money, 1984). Although paraphilias are often associated with sexual offending, the two terms are not synonymous. As Krueger and Kaplan (2001) point out, paraphilias often refer to a type of mental disorder. In contrast, "sexual offender" is a legal term that denotes individuals who have been convicted of a sexual offense. Nevertheless, many sexual offenders do meet diagnostic criteria for one or more paraphilic disorders and some individuals diagnosed with a paraphilic disorder have committed sexual offenses; thus, the two phenomena are by no means mutually exclusive (McElroy et al., 1999).

As a result of the association between paraphilic disorders and sexual offending, much of the research on paraphilias has been based on samples of convicted sexual offenders. Unfortunately, this leads to three major confounds. First, many sexual offenders were never formally diagnosed with a paraphilic disorder. Second, the generalizability of the samples to all individuals with paraphilic disorders is suspect, because individuals convicted of a sexual offense often represent the more severe end of the spectrum. Third, the veracity of self-reports by sexual offenders needs to be considered, because these individuals often have high motivations to appear less "deviant" in their sexual interests. As a result, they may under- and overreport certain fantasies and experiences. As a consequence of these issues, there is an increasing call for more research based on noncriminological samples (e.g., Kramer, 2011; Okami & Goldberg, 1992).

CLINICAL PICTURE

Exhibitionistic Disorder

Exhibitionism pertains to recurrent and intense sexual arousal from the exposure of one's genitals to an unsuspecting person, over a period of at least 6 months. It is one of the most commonly reported paraphilias (Firestone, Kingston, Wexler, & Bradford, 2006; Långström, 2010; Långström & Seto, 2006; Murphy, 1997). Exhibiting may consist of showing the genitals to, and/or actively masturbating in front of, a stranger. Often, the victim's shock is sexually arousing to the perpetrator and, in most cases, there is no other contact. To meet *DSM-5* criteria, the individual must either have acted on the sexual urges or fantasies or have experienced marked distress or interpersonal difficulty as a result of the sexual interest (APA, 2013).

Although primarily a disorder of men, female exhibitionism has been reported (e.g., Bader, Schoeneman-Morris, Scalora, & Casady, 2008; Federoff, Fishell, & Federoff, 1999). The majority of victims of exhibitionism are females, including both children and adolescents (Bader et al., 2008) although exhibitionists who prefer to expose themselves to children may have a different disorder from those who prefer to expose themselves to adults (Murphy & Page, 2008).

Exhibitionists are a heterogeneous group whose education, intelligence, and socioeconomic status do not differ from the general population (Blair & Lanyon, 1981). Initial investigations found high rates of shy and nonassertive personalities (Ellis & Brancale, 1956), but later studies utilizing more standardized assessment instruments did not find abnormal or specific personality patterns (Langevin, Paitich, Freeman, Mann, & Handy, 1978; Langevin et al., 1979; Smukler & Schiebel, 1975), nor did they find that psychopathology symptoms differed from other sexual or nonsexual offenders (Murphy, Haynes, & Worley, 1991; Murphy & Peters, 1992). Moreover, the majority of exhibitionists are married or in common-law relationships and enjoy nonpathological sexual relationships with their partners (Langevin & Lang, 1987; Maletzky, 1991).

Cox and Maletzky (1980) found that, in comparison to those with other paraphilias, exhibitionists were least likely to see their behavior as harmful to their victims—a factor likely to influence both motivations for, and success of, treatment. Relatedly, they are more likely to underreport or minimize their exhibitionistic and other paraphilic fantasies and behaviors (McConaghy, 1993; McConaghy, Blaszcyzynski, & Kidson, 1988), and among all individuals with paraphilias, exhibitionists were most likely to have committed other sexual offenses (Freund & Blanchard, 1986; Langevin & Lang, 1987).

Fetishistic Disorder

Fetishism pertains to recurrent and intense sexual arousal from either the use of nonliving objects or a highly specific focus on nongenital body part(s), present for at least 6 months and accompanied by clinically significant distress or impairment (APA, 2013). The objects are not limited to female clothing used in cross-dressing or to devices specifically designed for tactile genital stimulation, such as vibrators (Kafka, 2010). In the *DSM-5,* the object can be specified as either body parts or nonliving objects (or both).

Fetish objects can take many forms, including clothing (particularly underwear and stockings), footwear, diapers, gloves, and certain fabrics or materials such as rubber and leather. Sexual arousal may take the form of looking at, fondling, smelling, licking, sucking, cutting, burning, stealing, or seeing someone else dressed in the fetish objects (Chalkley & Powell, 1983). As with exhibitionism and, in fact, all the paraphilias, fetishism is largely a disorder found in men, although there are a few reports of women engaged in this behavior (Zavitzianos, 1971).

Frotteuristic Disorder

Frotteurism pertains to recurrent and intense sexual arousal from touching or rubbing against a nonconsenting person, over a period of at least 6 months. Unlike fetishism,

but similar to exhibitionism, clinically significant distress or impairment is not required if the individual has acted on the urges (APA, 2013). Although numerous researchers (e.g., Freund, 1990; Freund, Seto, & Kuban, 1996) include both touching and rubbing under the definition of frotteurism, others have differentiated frotteurism from toucherism (e.g., Adams & McAnulty, 1993; Kafka, 2010). The latter refers to sexual arousal from touching exclusively with the hands, rather than touching with, for example, the groin.

Frotteurism generally takes place in crowded places, such as on public transportation or on busy sidewalks, where escape for the frotteur is feasible (APA, 2000). Although engaging in frotteuristic activities, the frotteur "usually fantasizes an exclusive, caring relationship with the victim" (APA, 2000, p. 570). Frotteurism, as with most paraphilias, appears to occur mainly in men, although a few cases of frotteurism in women have been reported (Fedoroff et al., 1999; Kar & Koola, 2007). Krueger and Kaplan (1997) noted that "men who engage in frotteurism have large numbers of victims, are not often arrested, and, when apprehended, do not serve long sentences" (p. 145).

Very little published data exist on frotteurism. For example, Krueger and Kaplan (1997) found only 17 studies published on the topic between 1966 and 1997 on Psychlit and Medline. Our own search from 1997 to 2010 yielded only an additional 12 publications (see also Kafka, 2010).

Pedophilic Disorder

Pedophilia pertains to recurrent, intense sexually arousing fantasies, sexual urges, or behaviors involving sexual activity with a prepubescent child or children (generally age 13 years or younger) over a period of at least 6 months. To meet criteria, the individual must either have experienced consequent distress or interpersonal difficulty or have acted on the urges. Moreover, the individual must be at least 16 years of age and at least 5 years older than the prepubescent target of arousal (APA, 2013).

Unlike the other paraphilic disorders in the *DSM-5,* the Board of Trustees of the American Psychiatric Association did not accept the recommended changes to the diagnostic criteria for pedophilia (other than the name change from Pedophilia to Pedophilic Disorder). For example, the recommendation to have specifiers pertaining to the stage of puberty of the child for whom the patient has an erotic preference (e.g., Tanner stage 1 [prepubertal], Tanner stages 2–3 [early puberty] or both) were not approved. The Board of Trustees also chose to not include this proposed change in Section III of the Manual, in the section "Conditions for Further Study." It is of note that the Board of Trustees has not made public their decision to decline the recommendations made by the Paraphilias subworkgroup of the Sexual and Gender Identity Disorders Work Group (Zucker, 2013) and the decision has already been subjected to a charge of "politics" (Balon, 2014).

The reason that this change had been proposed is that there are now many children under the age of 13 years who are in early puberty and the introduction of this specifier would have more accurately acknowledged this empirical fact (see Blanchard, 2010a, 2013). It remains to be seen if, in court cases, it will be argued that a man with an erotic preference for children who are in early puberty, but who are under the age of 13 years, will be considered eligible for the diagnosis of pedophilic disorder.

Pedophilia is a term that is often incorrectly used interchangeably with *child molestation*. Although they can overlap, similar to the terms *paraphilia* and *sexual offender*, *pedophilia* describes the diagnostic term for a mental disorder, whereas *child molester* refers to any individual who has engaged in sexual activity with a prepubescent or pubescent child. As Barbaree and Seto (1997) point out, some pedophiles who have recurrent sexual fantasies or urges involving prepubescent children but without action would not be considered child molesters; conversely, individuals who have engaged in sexual activity with a minor once or even on occasion, but who do not experience recurrent fantasies, urges, or behaviors over a 6-month period, would not be diagnosed with pedophilia.

Individuals with pedophilia may be sexually aroused by girls, boys, both girls and boys, and even to both adults and children (APA, 2013). Furthermore, sexual arousal may be specific to children of particular ages. Although pedophilia involving girl victims is more frequent, the average number of victims is higher in pedophiles attracted to boys (Abel & Osborn, 1992). In addition, the rate of recidivism of male-preferential pedophilia is higher than that of female-preferential pedophilia (Abel & Osborn, 1992; Maletzky, 1993). Although originally believed to be a disorder specific to males, child sexual molestation by women has been reported in the literature (e.g., Cavanaugh-Johnson, 1988; Lane, 1991; Wijkman, Bijleveld, & Hendriks, 2010).

Compared to other paraphilias, an extensive literature exists for pedophilia (although much is based on child molesters who were never formally diagnosed with the disorder). A relatively high proportion of convicted child molesters experienced sexual abuse as children (50%, versus 20% in nonsex offenders; Dhawan & Marshall, 1996), as well as nonsexual abuse and neglect (Davidson, 1983; Finkelhor, 1979, 1984; Marshall, Hudson, & Hodkinson, 1993); however, child molesters did not suffer from higher rates of psychopathology or personality disturbances than nonmolesters (Abel, Rouleau, & Cunningham-Rathner, 1986; Mohr, Turner, & Jerry, 1964).

Finkelhor (1984) proposed that child molesters may suffer from a lack of empathy toward their victims that disinhibits restrictions the individual would otherwise have against offending. This finding has some support (Fernandez, Marshall, Lightbody, & O'Sullivan, 1999), although empathy toward adults and children more generally (i.e., not victims) does not differ from that of nonoffenders (Fernandez et al., 1999; Marshall, Hudson, Jones, & Fernandez, 1995). Thus, child molesters may push away empathic feelings toward their victims, but they do not suffer from any pervasive empathy deficits.

Sexual Masochism Disorder

Sexual masochism pertains to recurrent and intense sexual arousal from the act of being humiliated, beaten, bound, or otherwise made to suffer over a period of at least 6 months, and the person must suffer consequent distress or impairment in at least one important area of functioning. Furthermore, the sexual arousal must be in response to actual, not simulated, humiliation, bondage, or beatings although the use of pornography is sometimes an associated feature of the disorder (APA, 2013). In the *DSM-5*, asphyxiophilia can be denoted as a specifier (see Hucker, 2011).

Although pain through being slapped, spanked, or whipped is considered sexually arousing by most sexual masochists (Baumeister, 1989; Moser & Levitt, 1987), many sexual masochists use little or no pain (Baumeister & Butler, 1997), instead becoming aroused through loss of control by being bound or becoming aroused by carrying out humiliating acts such as wearing diapers, licking their partner's shoes, or having to display themselves while naked. Other masochistic activities include the use of electrical shocks, piercing (infibulation), being urinated or defecated on, being subjected to verbal abuse, self-mutilation, and oxygen deprivation (hypoxyphilia). Although many sexual masochists appear to practice these activities with safety in mind—by, for example, prearranging a signal with their partners to indicate when to stop (Scott, 1983; Weinberg & Kamel, 1983)—masochistic behaviors can lead to serious injuries and death (Agnew, 1986; Hucker, 1985). This is particularly true for activities involving oxygen deprivation, such as hanging or the use of ligatures, plastic bags, scarves, and chemicals.

The ratio of men to women who meet the criteria for this disorder is much smaller than that of the other paraphilias, with approximately 20 men having the disorder for every woman (APA, 2000). In community samples, the percentage of males who report masochistic sexual activities is higher than the percentage of females (2.2% vs. 1.3%) (APA, 2013). Gender differences in preferences for various masochistic activities reveal that pain and humiliation are the preferred forms of masochism for women; however, women prefer less-severe forms of pain than men (Baumeister, 1989). Being forced to be a slave and anal penetration have been found to be somewhat equally enjoyed by both sexes (Baumeister, 1989).

Interestingly, sexual masochism seems to be fairly modern when compared to the other paraphilias and also appears to be limited to Western cultures (Baumeister, 1989). Furthermore, it has been associated with increased socioeconomic functioning, with community samples of individuals who practice sexual masochism evidencing a higher level of education, higher income, and higher occupational status as compared to norms for the general population (for a review, see Weinberg, 2006). These findings have been corroborated by the demographics of those involved in S&M (sadism and masochism) organizations (Moser & Levitt, 1987; Scott, 1983; Spengler, 1977).

In line with the correlation between sexual masochism and socioeconomic status, research has found that sexual masochists are well-adjusted individuals who are often quite successful and above norms on measures of mental health (Cowan, 1982; Moser & Levitt, 1987; Scott, 1983; Spengler, 1977; Weinberg, 2006). In fact, one study that measured hormone levels before and after participation in consensual, sadomasochistic activities revealed reductions in cortisol following the sadomasochistic activities, indicating reduced physiological stress with this behavior (Sagarin, Cutler, Cuther, Lawler-Sagarin, & Matuszewich, 2009). Furthermore, this study also found that indices of relationship closeness increased following engagement in positively experienced sadomasochistic activities.

Some investigators have examined whether masochistic individuals enjoy pain, humiliation, and/or loss of control outside of sexual activity; however, there appears to be no relationship between sexual masochism and nonsexual forms of masochism (i.e., self-defeating behaviors or enjoyment of nonsexual painful behaviors such as going to the dentist; Baumeister, 1989, 1991; Baumeister & Scher, 1988; Berglas & Baumeister, 1993; Friedman, 1991; Scott, 1983; Weinberg, Williams, & Moser, 1984).

Sexual Sadism Disorder

Sexual sadism, in some ways the complementary opposite of sexual masochism, pertains to recurrent and intense sexual arousal from the physical or psychological suffering of another person over a period of at least 6 months. The urges and/or fantasies must have been carried out, must be distressing, or must cause interpersonal difficulty (APA, 2013).

As with sexual masochism, many individuals with sexual sadism engage in this behavior consensually and take precautions to ensure that their behavior does not exceed a certain threshold of pain or injury. However, sexual sadism can lead to serious injury or death, particularly when individuals with sexual sadism have a comorbid diagnosis of antisocial personality disorder (APA, 2013). Although the lay public often associates torture and cruelty to sexual sadism, it should be noted that these violent behaviors are not always accompanied by sexual arousal (Dietz, Hazelwood, & Warren, 1990; Hazelwood, Dietz, & Warren, 1992). Furthermore, it has been suggested that a sexual interest in power, and not the infliction of pain, is at the core of sexual sadism (Cross & Matheson, 2006). As with all the paraphilias, sexual sadism appears to be more common in men than in women (e.g., Breslow, Evans, & Langley, 1985, 1995).

Transvestic Disorder

Transvestic disorder pertains to recurrent and intense sexual arousal from cross-dressing, as manifested by fantasies, urges, or behaviors of at least 6 months, duration and is accompanied by significant distress or impairment (APA, 2013). Specifiers for this disorder are with fetishism or with autogynephilia (sexual arousal related to thoughts or images of self as female) (for a review of the term autogynephilia, see Lawrence, 2013).

Although in theory transvestic disorder can be present in both men and women, in practice, it is virtually never observed in women. Thus, the diagnostic criteria and the *DSM-5* text reflect this clinical reality. Moreover, the vast majority of males with transvestic disorder self-identify as heterosexual although some homosexual men have also been found to report sexual arousal to cross-dressing, albeit to a significantly lesser extent than heterosexual men (Blanchard & Collins, 1993; Docter & Prince, 1997).

Transvestic disorder can be associated with gender dysphoria and a desire to transition to the female gender role, particularly when it is associated with autogynephilia (sexual arousal in response to the idea or image of oneself as a women; Blanchard, 2005, 2010b; Lawrence, 2013).

The gender-related childhood and adolescent behaviors of men with transvestic disorder are consistent with those of other heterosexual men and unlike the childhood and adolescent behaviors often seen in homosexual men (Buhrich & McConaghy, 1985; Doorn, Poortinga, & Verschoor, 1994; Zucker & Bradley, 1995). Similarly, as adults, men with transvestic disorder generally have masculine occupations and hobbies (Chung & Harmon, 1994).

Transvestic disorder must be distinguished from transvestic behavior. Although the former involves sexual arousal in response to cross-dressing, this is not necessarily the case in the latter. Nonsexual transvestic behaviors can be found, for example, in

men who cross-dress for entertainment purposes (colloquially referred to as "drag queens").

Voyeuristic Disorder

Voyeurism pertains to recurrent and intense sexual arousal from observing an unsuspecting person who is naked, in the process of unrobing, or engaging in sexual activity as manifested by fantasies, urges, or behaviors. As with the other paraphilias, the *DSM-5* diagnostic criteria require the behavior to cause significant distress or interpersonal difficulty, or to be present in the form of actual voyeuristic activities (APA, 2013; Långström, 2010).

Abel et al. (1986) and Marshall and Eccles (1991) examined interpersonal skills and sexual functioning in voyeurs and found that these individuals have deficits in social and assertiveness skills as well as sexual knowledge, and that they also have higher rates of sexual dysfunctions and difficulties with intimacy than do nonvoyeurs. Nevertheless, approximately half have been found to be involved in marital relationships (Gebhard, Gagnon, Pomeroy, & Christenson, 1965).

Other Specified Paraphilic Disorder

This category applies to presentations in which symptoms of a paraphilic disorder are present, but the full criteria are not met for any of the disorders in the paraphilic disorders diagnostic class. It allows the clinician to communicate the specific reason why the individual does not meet criteria for a paraphilic disorder and record the specific reason, including the presence of a relatively uncommon paraphilia. Examples given in the *DSM-5* include telephone scatalogia, necrophilia, zoophilia, coprophilia, klismaphilia, and urophilia.

Unspecified Paraphilic Disorder

This diagnostic category is also used when the individual does not meet the full criteria for a paraphilic disorder and may be given in situations in which there is insufficient information to make a more specific diagnosis.

DIAGNOSTIC CONSIDERATIONS

In the *DSM-5,* a more formal distinction was made between the definition of a paraphilia (as earlier) and a paraphilic disorder. The latter requires that a paraphilia causes distress or impairment to the individual or a paraphilia whose satisfaction has entailed personal harm, or risk of harm, to others. Thus, a paraphilia is a necessary but not a sufficient condition for having a paraphilic disorder and a paraphilia by itself does not necessarily justify or require clinical intervention. The distinction between the ascertainment of a paraphilia and the diagnosis of a paraphilic disorder has already been applied in legal situations. The National Coalition for Sexual Freedom has documented that parents who engage in consensual bondage and discipline or sadomasochism are no longer being sanctioned for this conduct in child custody hearings (Wright, 2014).

In addition to this change, the *DSM-5* has introduced two specifiers that cut across all the paraphilias: in a controlled environment (noting that there may some environments in which the opportunity to enact a paraphilia is restricted), and in full remission (for at least 5 years while in an uncontrolled environment). The only exception to this pertains to pedophilic disorder: Because the Board of Trustees of the American Psychiatric Association preserved the diagnostic criteria as they appeared in *DSM-IV-TR,* these specifiers were not added (for a critique of this, see Balon, 2014).

Paraphilias must be distinguished not only from nonpathological sexual interests, but also from each other. For example, transvestic disorder must be distinguished from fetishistic disorder and sexual masochism disorder. Both transvestic disorder and fetishistic disorder can involve articles of feminine clothing, making it necessary to distinguish between a sexual interest in cross-dressing (necessary for a diagnosis of transvestic disorder) and a sexual interest in the articles of clothing themselves (necessary for a diagnosis of fetishistic disorder). Similarly, sexual masochism can involve humiliation via dressing in women's clothing, and thus must be distinguished from transvestic disorder and fetishistic disorder by the fact that the interest in cross-dressing seen in sexual masochism is specific to the humiliation felt while engaging in this behavior.

Distinguishing among the paraphilias can be complicated by the fact that the presence of one paraphilia is associated with a significantly elevated risk of having additional paraphilias (e.g., Kafka & Hennen, 1999; Price, Gutheil, Commons, Kafka, & Dodd-Kimmey, 2001). For example, transvestic disorder has been associated with autoerotic asphyxia—a form of sexual masochism—(Blanchard & Hucker, 1991), as well as with exhibitionism, voyeurism, and pedophilia (e.g., Långström & Zucker, 2005). Similarly, significant comorbidity has been found among exhibitionism, voyeurism, and frotteurism (Freund, 1990; Långström, 2010; Långström & Seto, 2006). In fact, in one study, only 10.4% of 561 nonincarcerated paraphiliacs had only one paraphilia (Abel, Becker, Cunningham-Rathner, Mittelman, & Rouleau, 1988).

Finally, paraphilic disorders need to be distinguished from other nonparaphilic disorders. For example, significant overlap can exist between transvestic disorder and gender dysphoria, whereby individuals may meet the criteria exclusively for either of these two diagnoses, but where it is also possible for individuals to meet criteria for both (APA, 2013).

As the *DSM-5* notes, other disorders that must be differentiated from the paraphilias include mental retardation, dementia, personality disorders, personality change due to a general medical condition, substance intoxication, mania, and schizophrenia.

EPIDEMIOLOGY

The incidence and prevalence of the paraphilias is unknown due to their secretive and often illegal nature. Therefore, frequency estimates are generally based on small, nonrepresentative samples, most often involving convicted sexual offenders. This research is, nonetheless, useful in deriving a preliminary indication of the occurrence of this group of disorders. Because many of these studies do not use *DSM* criteria, we summarize this literature without reference to the term *disorder* per se.

As previously noted, exhibitionism is one of the most common paraphilias and may be the most common sexual offense (e.g., Bartosh, Garby, Lewis, & Gray, 2003; Firestone et al., 2006). With respect to prevalence, studies have found that exhibitionism accounts for between one-third and two-thirds of all sexual offenses reported to police in Canada, the United States, and Europe (e.g., Gebhard et al., 1965; Smukler & Schiebel, 1975). Although estimates have varied, up to 20% of women may be victims of exhibitionism (Kaplan & Krueger, 1997; Meyer, 1995). Corroborating this high number of victims, Abel and Rouleau (1990) found that 25% of offenders in their outpatient clinics had a history of exhibitionism and that these 142 offenders reported a total of 72,074 victims. In one nonoffender study, 2% admitted to a history of exhibitionism (Templeman & Stinnett, 1991); however, in a more recent study involving a nationally representative sample of 2,450 adults in Sweden, more than 4% of males and 2% of females reported a history of at least one instance of exhibitionistic behavior for the purposes of sexual arousal (Långström & Seto, 2006).

Fetishism is a rare condition (APA, 2013). Chalkley and Powell (1983) reported that 0.8% of patients seen in three psychiatric hospitals over a period of 20 years met the criteria, and Curren (1954) found that only 5 out of 4,000 clients seen in private practice had a primary diagnosis of fetishism; however, as Mason (1997) notes, clinicians likely see only a small minority of the total number of individuals with fetishistic interests considering the wide proliferation of organizations and materials catering to these individuals. Nevertheless, it is unlikely that the majority of these individuals meet *DSM-IV-TR* criteria for fetishism, given that many do not experience distress or impairment.

Abel et al. (1988) interviewed 561 nonincarcerated paraphiliacs and found that 62 (11%) had a primary diagnosis of frotteurism, leading them to conclude that frottage is not the uncommon paraphilic act it has sometimes been touted to be. These rates are in line with other studies (Bradford, Boulet, & Pawlak, 1992; Kafka & Hennen, 2002), although even higher rates were found by Templeman and Stinnett (1991), who asked 60 college-aged men about frotteuristic activities and found that 35% indicated that they had engaged in frottage. Interestingly, a study of 33 adult men and 28 adult women in India revealed higher rates of reported sexual interests in frotteurism in women (14.3%) than in men (9.1%) (Kar & Koola, 2007); this finding is very surprising given that paraphilias are generally considered to be very uncommon in women, with the exception of sexual masochism.

Although a substantial amount of research has been conducted on pedophilia, its prevalence is unknown. Seto (2009) has extrapolated that the upper limit for the prevalence of pedophilia is likely around 5%. This is based on the fact that several small convenience-sample surveys with men have revealed rates of between 3% to 9% for self-reported sexual fantasies or sexual contact involving prepubescent children (e.g., Fromuth, Burkhart, & Jones, 1991; Templeman & Stinnett, 1991), but also on the fact that these rates are likely to overestimate the prevalence of pedophilia because these surveys did not assess the intensity, persistence, or presence of distress/impairment related to the sexual fantasies/behaviors.

Baumeister (1989) estimated that between 5% and 10% of the population has engaged in some form of masochistic activities based on a literature review of findings from other studies. He further hypothesized that double this number have had

fantasies about sexual masochism but that less than 1% of the population likely engages in masochistic sexual activities on a regular basis.

Since Baumeister's (1989) review, more recent studies have been conducted with both clinical and nonclinical populations. In studies with sexual offenders, the rates of sexual masochism have ranged from 2% (Becker, Stinson, Tromp, & Messer, 2003) to just over 5% (Hill, Habermann, Berner, & Briken, 2006). Higher percentages—but still in line with the review by Baumeister (1989)—have been found in studies of outpatient males seeking treatment for paraphilic or paraphilia-related disorders, with between 9% and 11% of the samples meeting criteria for sexual masochism (Kafka & Prentky, 1994; Kafka & Hennen, 2002, 2003). With respect to nonclinical populations, an Australian study that assessed participation in bondage, discipline, sadomasochism, dominance, or submission via telephone survey revealed that 2.0% of men and 1.4% of women acknowledged having engaged in these activities at some point in their lives (Richters, Grulich, de Visser, Smith, & Rissel, 2003).

Paraphilic interests, in general, are rarely known to occur in women, with the exception of sexual masochism. In line with the notion that sexual masochism is not specific to males, a recent literature review of studies that have assessed women's rape fantasies revealed that between 31% and 57% of women have had sexual fantasies involving forced sexual activities, and that, of these women, 9% to 17% reported that these fantasies were either their most frequent or their most preferred fantasies (Critelli & Bivona, 2008).

Several studies have been conducted on the extent of sexual sadism in clinical and nonclinical samples. Of studies with convicted sexual offenders, rates of sexual sadism have ranged substantially, from 4% to 9% in some studies (e.g., Becker et al., 2003; Elwood, Doren, & Thornton, 2010; Levenson, 2004) to upwards of 35% in other studies (e.g., Berger, Berner, Bolterauer, Gutierrez, & Berger, 1999; Hill et al., 2006).

In a study of 561 adult males seeking outpatient treatment for possible paraphilias, 28 (5%) of participants met the criteria for sexual sadism (Abel et al., 1987; Abel et al., 1988), consistent with a more recent study with 120 outpatient males with paraphilias or paraphilia-related disorders, 60 of whom were sex offenders (Kafka & Hennen, 2002, 2003). Another study of 63 outpatient males found 12% of the sample meeting criteria for sexual sadism (Kafka & Prentky, 1994).

With respect to nonclinical samples, Hunt (1974) surveyed both men and women on their sexual experiences and found that 5% of men and 2% of women endorsed becoming sexually aroused to inflicting pain on others. Crepault and Couture (1980) assessed rates of sexually sadistic fantasies in a community sample of men and found that 11% had fantasies of beating up a woman and 15% had fantasies of humiliating a woman. Arndt, Foehl, and Good (1985) found that half of their sample of men and one-third of their sample of women indicated having had prior fantasies of tying up their partners.

Along with exhibitionism, voyeurism is one of the most common paraphilias and one of the most common sexual offenses (e.g., Bradford et al., 1992; Långström & Seto, 2006). In the study by Långström and Seto (2006), involving 2,450 adult men and women from a nationally representative sample in Sweden, 12% of men and 4% of women acknowledged at least one instance of sexual arousal in response to viewing unsuspecting individuals engaging in sexual activities. Much higher rates were found in a study of 33 adult men and 28 adult women in India (Kar & Koola, 2007), where

55% of the men and 25% of the women in the sample had engaged in voyeuristic activities. Furthermore, 3% of these men reported that voyeurism was a necessary component for sexual gratification. These high rates are in line with at least one study of 60 male college students in the United States, in which 42% engaged in voyeuristic activities and 53% reported an interest in voyeurism (Templeman & Stinnett, 1991). Meyer (1995) has posited that up to 20% of women have been targeted by voyeurs.

In a population-based study on transvestic fetishism, Långström and Zucker (2005) found that 2.8% of 1,279 Swedish men and 0.4% of 1,171 Swedish women reported sexual arousal in response to cross-dressing. The percentage for men is consistent with another, subsequent study, which also found that 3% of a small sample of men ($n = 33$) acknowledged engaging in cross-dressing for sexual purposes (Kar & Koola, 2007). Interestingly, this latter study found a higher rate of transvestism (7.1%) in the 28 women in the sample.

PSYCHOLOGICAL AND BIOLOGICAL ASSESSMENT

Assessment strategies include questionnaires and self-report measures, as well as objective, physiological measures, such as the plethysmograph, the polygraph, and measures of visual reaction time. Two challenges inherent in measuring paraphilic interests are (1) the fact that sexuality is typically a private matter and many individuals are uncomfortable discussing their interests and/or behaviors that carry a social stigma and (2) the ethical aspects of assessment whereby some techniques are invasive and/or involve the presentation of potentially disturbing sexual stimuli. All of these techniques suffer from problems with reliability, validity, and vulnerability to dissimulation to varying degrees. Therefore, no one technique should be used in isolation.

Self-Report Measures

One of the most widely used self-report measures is the Clarke Sexual History Questionnaire for Males (Paitich, Langevin, Freeman, Mann, & Handy, 1977), a 190-item questionnaire that assesses a wide range of sexual experiences, including paraphilic experiences, their frequency, and their age of onset. Another self-report measure, the Multiphasic Sex Inventory (Nichols & Molinder, 1984, 1992), assesses paraphilic sexual preferences, sexual knowledge, and sexual dysfunction. The Wilson Sex Fantasy Questionnaire (Wilson, 1978) is a further standardized, commonly used instrument. Unfortunately, all these measures have the potential for biased or dishonest responses.

Card-sort techniques contain rating scales composed of pictorial or written sexual stimuli that individuals are asked to view and then rate according to the degree of sexual arousal elicited. Examples include the Sexual Interest Card Sort Questionnaire (Holland, Zolondek, Abel, Jordan, & Becker, 2000) and Laws' (1986) Sexual Deviance Card Sort. Clinicians can also develop their own card sorts specific to what they know about a client, or they can ask their clients to record their daily sexual fantasies and urges and then rate the corresponding degree of sexual arousal (Maletzky, 1997).

A review by Schiavi, Derogatis, Kuriansky, O'Connor, and Sharpe (1979) of 50 self-report instruments used with sexual offenders found little evidence for their validity;

however, their usefulness may lie in their ability to be used in conjunction with historical information that allows examination of inconsistencies (Kaplan & Krueger, 1997) or bias (Abel & Rouleau, 1990).

PSYCHOPHYSIOLOGICAL ASSESSMENT TECHNIQUES

Because of the difficulties with self-report, many clinicians and researchers depend on objective measures. Of these, phallometric assessment is considered to be the most reliable and valid and the least prone to dissimulation (Quinsey, 1988; Quinsey & Earls, 1990; Seto, 2001). This technique involves the psychophysiological recording of sexual arousal through a device that measures either volumetric or circumferential changes in penile tumescence in response to sexual stimuli. The stimuli can take various forms, such as videos, audiotapes, photographs, and written text. Consistent increases in penile tumescence to specific sexual stimuli relative to other sexual and nonsexual stimuli are considered to indicate sexual preferences for those stimuli (Freund, 1963). The use of stimuli depicting individuals of all ages and both sexes, engaged in various sexual and nonsexual activities, reliably discriminates sexual from nonsexual offenders, including child molesters and non-child molesters (Barbaree & Marshall, 1989; Freund & Blanchard, 1989); rapists and nonrapists (Harris, Rice, Chaplin, & Quinsey, 1999; Lalumiere & Quinsey, 1994); men who admit to sadistic fantasies, cross-dress, or expose their genitals in public from men who do not (Freund, Seto, & Kuban, 1996; Seto & Kuban, 1996); and incest offenders and nonoffenders (Barsetti, Earls, & Lalumiere, 1998; Chaplin, Rice, & Harris, 1995). Phallometry also has high predictive power for sexual and violent recidivism (Malcolm, Andrews, & Quinsey, 1993; Rice, Harris, & Quinsey, 1990; Seto, 2001), similar to that of psychopathy diagnoses and criminal history (Hanson & Bussiere, 1998). Sexual interests, as measured through phallometric testing, are considered to be the most consistently identifiable distinguishing characteristics of sexual offenders compared to general psychopathology, empathy, and social skills (Quinsey & Lalumiere, 1996; Seto & Lalumiere, 2001).

Phallometric testing is not without its criticisms. For example, group discrimination is not perfect, with the distributions of phallometric scores overlapping between sex offenders and nonoffenders (Seto, 2001). Furthermore, although the specificity of phallometry is very high (i.e., the test is able to accurately identify men who have not committed a sexual offense as nondeviant 90% to 97.5% of the time), the sensitivity of the test (i.e., the ability of the test to identify men who have committed a sexual offense as deviant) appears to be only between 44% and 50% (Freund & Watson, 1991; Lalumiere & Quinsey, 1993). In addition, in 21% of participants assessed with phallometric testing, no clear diagnosis with respect to paraphilic sexual preferences was possible (Freund & Blanchard, 1989).

Furthermore, a lack of standardization in stimuli, testing procedures, and data analysis results in considerable variability in procedures, data interpretation, and outcome across phallometric laboratories (Howes, 1995), making it difficult to evaluate the technical adequacy of different phallometric studies, replicate experiments, and account for discrepancies between studies (Schouten & Simon, 1992). There are also ethical concerns because sexual stimuli that depict violent sexual behavior or sexual images of children are usually presented. Finally, although phallometric testing

is much less susceptible than self-report to response bias or dissimulation, some participants can alter their physiological responses in a socially desirable direction (see Freund, Watson, & Rienzo, 1988, for a review; Lalumiere & Earls, 1992), an issue that has an impact on the procedure's sensitivity. Furthermore, the ability of participants to control, or alter, their physiological responses increases with subsequent testing (Quinsey, Rice, & Harris, 1995), suggesting that multiple assessments give participants the opportunity to learn how to alter their responses so they appear less sexually deviant (Lalumiere & Harris, 1998).

The polygraph (also known as the "lie detector") is another psychophysiological assessment technique used with individuals who have been accused or convicted of a sexual offense. However, unlike the plethysmograph, which is used to assess current sexual interests, the polygraph assesses past sexual behaviors and deceitfulness by measuring galvanic skin response, heart rate, blood pressure, and respiration. Changes in arousal are associated with involuntary responses to fear, based on the assumption that when people lie, they fear that their lie will be discovered, leading to measurable physiological increases. As Branaman and Gallagher (2005) indicate, the validity of the polygraph largely depends on the types of questions asked during the assessment. This has led to significant caution because the implications of incorrectly identifying someone as having committed sexual offenses are numerous and severe. Furthermore, skeptics note that some individuals may feel coerced into admitting to offenses they never committed (Cross & Saxe, 1992, 2001). Because of these concerns, the polygraph is not generally admissible in court.

Another objective assessment is visual reaction time (also referred to as viewing time). Similar to phallometric testing, this strategy involves showing pictures of various sexual and nonsexual stimuli. Participants are informed that the technique assesses sexual interests through their self-reported ratings of sexual attractiveness to each picture. However, participants do not know that the procedure involves the unobtrusive recording of the length of time they view each stimulus. The technique is based on findings that individuals view images they find sexually stimulating longer than those they do not (Lang, Searles, Lauerman, & Adesso, 1980; Quinsey, Rice, Harris, & Reid, 1993). Visual reaction time has similar reliability and validity as phallometric testing (Abel, Huffman, Warberg, & Holland, 1998; Letourneau, 2002), with the added advantages of greater efficiency, less intrusiveness, and less technological complexity than phallometry (Abel et al., 1998; Harris, Rice, Quinsey, & Chaplin, 1996). Because the technique is less intrusive and thus less ethically controversial, it has also been used with adolescent sexual offenders with promising results (Abel et al., 2004).

ETIOLOGICAL CONSIDERATIONS

Numerous theories have been proposed to explain how the paraphilias develop; however, empirical evidence is either lacking or contradictory, and, as a result, no individual theory satisfactorily explains the development of paraphilic sexual interests. Nevertheless, knowledge of these theories provides some insight into current thinking about how paraphilic sexual disorders develop and the rationale behind various treatment approaches.

NEUROANATOMY AND NEUROBIOLOGY

Cases in which individuals developed paraphilic sexual interests following brain injuries and degenerative brain diseases (for a review, see Langevin, 1990) have led to hypotheses that the paraphilias may be caused by certain neurological abnormalities, particularly temporal lobe and limbic area abnormalities. Unfortunately, these findings are not uniform and they fail to account for a large number of individuals with paraphilias (Hucker et al., 1988; O'Carroll, 1989; Tarter, Hegedus, Alterman, & Katz-Garris, 1983). Further, numerous studies have found that temporal lobe disorders are generally associated with hyposexuality, not hypersexuality (Miller, Darby, Swartz, Yener, & Mena, 1995; Rosenblum, 1974).

New research suggests possible neurobiological underpinnings of paraphilic interests. In particular, research by Cantor et al. (2008), which compared the MRI scans of a sample of 65 pedophiles to a sample of 62 nonsexual offenders, found that pedophilic men had significantly less white matter in the superior fronto-occipital fasciculus and the right arcuate fasciculus regions of the brain. These regions of the brain, located in the temporal and parietal lobes, are composed of axons that connect to other brain regions, thereby suggesting differences in the connectivity of the various regions of the brain in pedophiles versus nonpedophiles. Specifically, Cantor et al. (2008) surmised that because the superior fronto-occipital fasciculus and arcuate fasciculus connect those regions of the brain that respond to sexual cues, pedophilia may be the result of a partial disconnection within the network that recognizes sexually relevant stimuli.

As Cantor et al. (2008) pointed out, it must be acknowledged that it is unknown whether these differences are the cause or the result of pedophilia, or due to an unknown third variable. However, given that these two regions of the brain are not generally associated with changes following environmental stimulation, the possibility that these changes are the result of pedophilia is unlikely. Furthermore, the relatively lower volumes of white matter found in pedophiles is congruent with neuropsychological findings that pedophilic men have lower IQs (Cantor, Blanchard, Christensen, Dickey, & Klassen, 2004; Cantor, Blanchard, Robichaud, & Christensen, 2005), poorer visuospatial and verbal memory abilities (Cantor et al., 2004), higher rates of being non-right-handed (Cantor et al., 2004; Cantor, Blanchard, Robichaud, & Christensen, 2005), higher rates of head injuries that resulted in unconsciousness in childhood (Blanchard et al., 2002; Blanchard et al., 2003), and higher rates of having failed grades in school or having been placed in special education programs (Cantor et al., 2006), than nonpedophilic men. These characteristics may also be the result of reduced white matter volume and, in the case of handedness, become apparent very early in life (i.e., in utero). As such, the possibility that pedophilia leads to a lower volume of white matter over time is unlikely, and it is more likely that pedophilia is the result of an anomaly in early neurodevelopment (Blanchard et al., 2002).

LEARNING, MODELING, AND LIFE EVENTS

Behavioral theories of paraphilias have garnered much attention from clinicians and researchers, and have shaped many of the psychotherapeutic approaches used to treat paraphilic interests. Behavioral theories posit that paraphilias develop through operant or classical conditioning in which the object of paraphilic attention becomes paired

with sexual arousal, resulting in abnormal arousal patterns. In essence, sexual arousal becomes the conditioned response to the paraphilic target and is reinforced through masturbation and orgasm.

Research by Rachman (1966; see also Rachman & Hodgson, 1968) demonstrated that sexual arousal can, in fact, be conditioned; they conditioned a sexual response to a picture of a pair of boots by pairing the picture of the boots with photographs of nude adult women. However, the responses were easily extinguished, leading others to argue that the behavioral theory is not sufficient on its own to explain the maintenance of such behaviors throughout an individual's life (Bancroft, 2009).

Modeling and the effects of early life events have also been hypothesized to play a causal role. The belief that negative and disruptive early childhood and family functioning may lead to paraphilias comes from research indicating high rates of childhood abuse (both sexual and nonsexual), neglect, and disturbed family relations in paraphilic individuals (e.g., Marshall et al., 1993; Saunders, Awad, & White, 1986). Marshall et al. suggested that these negative experiences serve as templates for future relationships, leading to distrust or ambivalence with appropriate partners and teaching individuals to be abusive toward others. McGuire, Carlisle, and Young (1965) more specifically hypothesized that individuals who experience sexual abuse as children go on to use thoughts of the abuse during masturbation in adolescence, thus pairing abusive thoughts with the pleasure of masturbation, and leading to specific, paraphilic sexual preferences. These hypotheses, however, fail to account for the many individuals who have experienced abuse and dysfunctional family relationships who do not go on to develop paraphilias and, conversely, the many individuals with paraphilias who have no history of familial instability or victimization (Murphy, Haynes, & Page, 1992; Murphy & Smith, 1996).

Cognitive Influences

Cognitive-behavioral theories have emphasized the role of cognitions in the etiology of sexual offending (e.g., Ward, Hudson, & Marshall, 1995). Cognitive distortions include beliefs and ways of thinking that minimize or deny harm and attribute blame to victims or to other external factors, resulting in a lack of empathy toward victims. These distorted beliefs facilitate and justify further sexual offending (Abel, Becker, & Cunningham-Rathner, 1984) and have, thus, become the target of most treatment efforts with sexual offenders. However, evidence is lacking that these cognitions cause paraphilic sexual interests to develop. In fact, even the extent to which they cause initial instances of sexual offending, versus emerging after the fact, remains unclear. Of note is that researchers have found that child molesters are not lacking in general empathy (i.e., they have not been found to be less empathic compared to non-child molesters), but that they are lacking in specific empathy toward their victims (Marshall, Jones, Hudson, & McDonald, 1994).

COURSE, PROGNOSIS, AND TREATMENT

Paraphilias most commonly first appear in adolescence (e.g., Abel, Osborn, & Twigg, 1993; McConaghy, 1993; Zucker & Bradley, 1995), with charges and convictions most frequently occurring in early adulthood (e.g., Berah & Meyers, 1983). The course has

generally been found to be chronic (e.g., Gosselin & Wilson, 1980), and, at least in the case of sexual sadism, the severity may increase over time (APA, 2000).

Due to ethical and methodological limitations in conducting empirical investigations of treatment efficacy with paraphilic individuals (such as randomly assigning convicted offenders to a no-treatment control group), and because most paraphilias have extremely low base rates, leading to difficulties with acquiring adequate sample sizes, efficacy rates for the treatment of the paraphilias has not been conclusive. In fact, some professionals have argued that there currently is no empirical basis indicating that treatment for sexual offenders is superior to placebo (e.g., Furby, Weinrott, & Blackshaw, 1989). Treatment of paraphilias with nonoffending individuals is often focused on helping them understand that paraphilias are lifelong and that people do not choose what will interest them sexually. In addition, treatment may focus on how the interests can be managed in ways that do not involve illegal activities or risks to physical health and safety, and in ways that do not affect social and/or occupational functioning.

CASE STUDY

John is a 21-year-old, single, heterosexual, Caucasian male who resides with his parents and two younger siblings. He has a college diploma and is currently employed in the sales industry. John's probation officer referred John to a behavioral sexology clinic following John's conviction for committing an indecent act (also known as "indecent exposure" or "public indecency"). John was charged and convicted of committing an indecent act after he drove his car alongside two females, ages 14 and 20, exposed his penis, and then masturbated to the point of ejaculation before driving away. John has no criminal record for any prior sexual or nonsexual offenses; however, John acknowledged a sexual interest in exhibitionism and a prior history of exposing himself to strangers. He reported that he spontaneously began to have fantasies about exposing himself to unsuspecting women when he was approximately 18 or 19 years of age. His fantasies of exhibitionism involve the unsuspecting woman becoming intrigued and aroused by his exhibitionism and this leading to consensual partnered sexual activities. At the same time, John acknowledged that, although this is his fantasy, he has never actually believed that this would happen in reality.

John reported that he exposed himself for the first time when he was 19 years old. He was driving in his car, with no prior intention of exposing himself, when he drove past an attractive, adult female walking on the street. John reported that he developed a strong urge to expose himself to her. He maneuvered his car in such a way that she walked by him and could see in his window, and he then masturbated to the point of ejaculation. According to John, the female noticed what he was doing but gave no reaction. John felt very guilty after the incident. Nonetheless, he noticed that his fantasies and urges to expose himself increased.

John's second instance of exposing himself occurred when he was in college. He was in the college library when he saw an attractive female studying in a study carrel across from him. John once again exposed his penis and masturbated to the point of ejaculation, after which he ran out of the library and again felt very guilty.

With respect to the incident that resulted in John's conviction and subsequent referral to the behavioral sexology clinic, John reported that he had purposely gotten in his car and driven around searching for an attractive female to expose himself to after experiencing strong urges to do so. He reported that he then saw the two victims, the older of whom he found attractive. He pulled up to them, exposed himself, and masturbated to the point of ejaculation. He then drove away but was contacted by police an hour later.

John expressed a lot of guilt about his exhibitionistic urges and behaviors. He acknowledged that he continues to have urges to expose himself since the index offense but reported that he has been able to refrain from acting out on the urges by reminding himself of his arrest and conviction. At the same time, he expressed concern that thinking of the index offense may not be enough to resist his urges in the future.

With respect to other sexual interests, John reported that he is sexually attracted exclusively to females who are approximately his age. He reported no sexual attraction to prepubescent or pubescent females. He similarly reported that he has no sexual interest in cross-dressing, leather, latex, rough or violent sexual behavior, or being humiliated. He reported no interest in voyeurism beyond viewing "amateur" pornographic videos that advertise that the performers are unaware of being filmed. He reported no concerns pertaining to sexual functioning or gender identity.

Assessment involved a comprehensive psychosexual history, including information about his exhibitionistic fantasies, urges, and behaviors, information about other paraphilic and nonparaphilic interests and behaviors, general mental and physical health, and social and interpersonal functioning. Through this psychosexual history, John met *DSM-IV-TR* criteria for exhibitionism.

John did not report any other paraphilic sexual interests; however, given the nature of the referral and the additional fact that one of the two victims of the index offense was 14 years of age, corroborative objective assessment via phallometric testing was deemed appropriate. Phallometric testing was not indicative of a sexual interest in either prepubescent or pubescent children. Thus, John's final diagnosis was exhibitionism, and it was concluded that he could potentially benefit from participation in cognitive-behavioral/relapse prevention treatment for his sexual offending behaviors.

SUMMARY

Often associated with sexual deviance and sexual offending, the paraphilias are one of the most controversial groups of disorders. This controversy stems from disagreements over such issues as whether the paraphilias should be categorized as mental disorders or instead be seen simply as variants of human sexuality; arguments over why certain sexual behaviors are included under the paraphilias (such as fetishism), whereas others are not (such as rape); and arguments over the specific diagnostic criteria for each of the paraphilias. This controversy is furthered by the limited amount of sound empirical research—particularly epidemiological research—with individuals with these conditions. However, assessment and treatment of the paraphilias have advanced significantly toward more effective, efficient, and ethical techniques.

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CHAPTER 16

Gender Dysphoria

ANNE A. LAWRENCE and KENNETH J. ZUCKER

DESCRIPTION OF THE DISORDER

The term *gender dysphoria* (GD) denotes discomfort with one's biological sex or assigned gender. GD is the defining characteristic of a category of psychosexual disorders in which affected persons are "intensely and abidingly uncomfortable in their anatomic and genetic sex and their assigned gender" (Fisk, 1974b, p. 10). The most widely recognized and severe manifestation of GD is *transsexualism*, in which affected persons express an intense and persistent desire to live and be recognized as members of the other sex and to make their bodies resemble those of the other sex through hormonal and surgical treatment. Less severe and less widely known manifestations of GD also exist, however, and may be more prevalent than transsexualism.

History and Terminology

Individuals who wish to live and be recognized as members of the other sex have been recognized since antiquity in many different societies worldwide (Green, 1969). The German physicians Krafft-Ebing (1903/1965) and Hirschfeld (1910/1991) described patients who would now be diagnosed as suffering from GD. Christine Jorgensen's widely reported sex reassignment in 1952 brought the phenomenon of transsexualism to public attention in Western countries (Meyerowitz, 2002). By the 1960s, academic medical centers in the United States and Western Europe had begun to offer hormonal and surgical sex reassignment to carefully selected patients. In 1980, conditions involving GD were first recognized as psychiatric diagnoses in the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-III*; American Psychiatric Association [APA], 1980).

Historically, the term GD has been used in several different ways, which has sometimes caused confusion. Fisk, who introduced the term, offered three slightly different definitions: He originally defined GD as discomfort with *both* biological sex and assigned gender (Fisk, 1974b), but in subsequent definitions focused primarily on either biological sex ("displeasure with the sex of [one's] genital anatomy, the chromosomes, and the endocrine secretions"; Laub & Fisk, 1974, p. 390) or on assigned

gender ("dysphoria concerning the individual's gender of assignment or rearing"; Fisk, 1974a, p. 388). Blanchard's definitions of GD sometimes emphasized only discomfort with biological sex ("persistent discontent with the primary or secondary sexual characteristics of one's body"; Blanchard, 1993b, p. 70) but at other times also emphasized cross-gender aspirations ("discontent with one's biological sex, the desire to possess the body of the opposite sex, and the desire to be regarded by others as a member of the opposite sex"; Blanchard, 1993a, p. 301). The *DSM-IV* (APA, 1994) and *DSM-IV-TR* (APA, 2000) stated that intense discomfort with *either* biological sex or assigned gender role could justify a diagnosis of GD ("persistent aversion toward some or all of those physical characteristics or social roles that connote one's own biological sex"; APA, 2000, p. 823). Note that, in at least some of these definitions, discomfort with biological sex characteristics alone was considered sufficient to diagnose GD; cross-gender identification was not always explicitly required.

More recent definitions of GD, in contrast, have deemphasized discomfort with biological sex characteristics and have focused almost exclusively on discordance between assigned sex and *gender identity* ("an individual's identification as male, female, or, occasionally, some category other than male or female"; APA, 2013, p. 451). The World Professional Association for Transgender Health (WPATH), for example, defined GD as "discomfort or distress that is caused by a discrepancy between a person's gender identity and that person's sex assigned at birth (and the associated gender role and/or primary and secondary sex characteristics)" (WPATH, 2011, p. 5). Two succinct definitions of GD that occur in the *DSM-5* (APA, 2013) do not even mention biologically based discontent or distress ("affective/cognitive discontent with the assigned gender" and "distress that may accompany the incongruence between one's experienced or expressed gender and one's assigned gender"; APA, 2013, p. 451). Although the term *experienced or expressed gender* is never formally defined in the *DSM-5,* its usage therein suggests that it is synonymous with *gender identity* (e.g., "experienced gender may include gender identities beyond binary stereotypes"; APA, 2013, p. 453).

The *DSM-III, DSM-III-R, DSM-IV,* and *DSM-IV-TR* all categorized psychosexual disorders involving GD under the overarching category of *gender identity disorders* (GIDs), because an "incongruence between anatomic sex and gender identity" (APA, 1980, p. 261) was considered to be the defining characteristic of these conditions. The *DSM-5* made GD both the overarching category and a specific diagnosis within the category, because "the current term [GD] is more descriptive than the previous DSM-IV term *gender identity disorder* and focuses on dysphoria as the clinical problem, not identity per se" (APA, 2013, p. 451; see also Zucker et al., 2013). The *DSM-5* nevertheless makes it clear, however, that a problem involving one's gender identity—now framed as an "incongruence between one's experienced/expressed gender and assigned gender" (APA, 2013, p. 452)—"is the core component of the diagnosis" (p. 453). Thus, the *DSM-5* apparently still conceptualizes GD as a disorder *primarily involving* gender identity, if not a disorder *of* gender identity.

In all of these *DSM* editions, adult and adolescent psychosexual diagnoses involving GD or GIDs have usually consisted of one principal or prototypical diagnosis with specific diagnostic criteria and one or more residual diagnoses, usually without specific criteria. In the *DSM-III* (APA, 1980), the principal diagnosis was Transsexualism and the residual diagnosis was Atypical Gender Identity Disorder. In

the *DSM-III-R* (APA, 1987), the principal diagnosis remained Transsexualism, and the residual diagnoses became Gender Identity Disorder of Adolescence or Adulthood, Nontranssexual Type (GIDAANT)—the only residual diagnosis to have specific criteria—and Gender Identity Disorder Not Otherwise Specified (GIDNOS). In the *DSM-IV* (APA, 1994) and *DSM-IV-TR* (APA, 2000), GID became the principal diagnosis and the only residual diagnosis was GIDNOS. The *DSM-5* continues this general pattern: The principal diagnosis is GD and the residual diagnoses are other specified GD and unspecified GD. Principal diagnoses involving gender identity problems have become progressively more encompassing in successive versions of the *DSM*: Many clinical presentations that once would have received a residual diagnosis (e.g., GIDAANT or GIDNOS) would now receive the principal diagnosis, GD.

Although *transsexualism* is no longer an official *DSM* diagnosis, many clinicians continue to use the term, in part because it remains an official diagnosis in the *International Classification of Diseases* (World Health Organization, 1992). Some experts consider transsexualism to be synonymous with "severe GD" (e.g., Blanchard, 1993c). The distinction between transsexualism and GD may be of limited practical importance, because much of the research relevant to understanding GD in adults has involved persons who would meet diagnostic criteria for transsexualism by most definitions. Adults with severe GD, especially those who request or have completed sex reassignment, are commonly referred to as male-to-female (MtF) and female-to-male (FtM) transsexuals.

The terms *transgender* and *transgenderism* are used informally to describe persons who report or exhibit significant cross-gender or gender-variant identity or behavior, regardless of whether they meet diagnostic criteria for GD or transsexualism. Some of these individuals, including some who meet diagnostic criteria for GD, may explicitly identify as transgender persons.

CLINICAL PICTURE

Typical Clinical Presentations

Dislike for one's primary or secondary sex characteristics, discomfort with one's assigned gender or associated gender role, identification with the other gender, and requests for approval for hormonal and surgical sex reassignment are the most frequent presenting complaints of adult patients with GD. Adults with GD sometimes present initially with other clinical concerns, however, including paraphilias, sexual dysfunctions, depression, or other general psychiatric conditions (Levine, 1993).

Persons with GD usually identify with the other sex; they may want the anatomy, the gender role, or the sexuality of the other sex, or any combination of these (Carroll, 1999). Persons with severe GD or transsexualism typically want both the anatomy and the gender role of the other sex (Deogracias et al., 2007; Singh et al., 2010). As noted earlier, an intense feeling of "wrong embodiment," manifesting as discontent with sexed body characteristics and a strong desire to acquire the anatomy of the other sex, has sometimes been considered the essential feature of severe GD and especially of transsexualism (Blanchard, 1993b; Bower, 2001; Laub & Fisk, 1974; Prosser, 1998). However, not all patients with GD experience intense anatomic dysphoria; some

primarily desire to enact the gender role or sexuality of the other sex and are unconcerned or ambivalent about acquiring the anatomic features of the other sex.

Less Common Clinical Presentations

Rarely, persons with GD may identify with what the *DSM-5* calls "some alternative gender" that corresponds to neither their assigned sex nor the other sex. Examples would include males who desire castration and who identify as *eunuchs* (Johnson, Brett, Roberts, & Wassersug, 2007; Johnson & Wassersug, 2010) and persons who want some combination of the secondary sex characteristics of both sexes who identify as *she-males*, *trans* persons, or *transgender* persons (Davidmann, 2010).

In some cases, persons with various *disorders of sex development* (DSDs; formerly known as *intersex* conditions) experience distress due to an incongruence between their gender identity and their assigned gender. These individuals can be given the principal diagnosis of GD in the *DSM-5,* with the assignment of the newly added DSD specifier. In previous editions of the *DSM,* the presence of a DSD or intersex condition was considered an exclusion criterion for the principal GID diagnosis, and gender dysphoric persons with these conditions could only receive a residual diagnosis (e.g., GIDNOS). Notwithstanding this change, the recommendation made by Mazur, Colsman, and Sandberg (2007) still seems advisable: Because of probable but still incompletely understood differences in the etiology and presentation of GD "in physically typical persons (i.e., transsexuals) and in those with intersex conditions . . . , it would be prudent to consider them as separate entities when initiating an evaluation" (p. 236). Richter-Appelt and Sandberg (2010) similarly emphasized that "the etiology, natural history, and response to treatment may be quite different" (p. 98) in gender dysphoric persons with and without DSDs. For example, in persons without DSDs, GD usually appears during childhood and is more prevalent in males than in females; in persons with recognized DSDs, GD more commonly appears during adolescence and is more prevalent in female-assigned than male-assigned persons.

Discussion of the prevalence and manifestations of GD in specific DSD syndromes is beyond the purview of this chapter, but useful summaries and reviews exist (e.g., Mazur et al., 2007; Steensma, Kreukels, de Vries, & Cohen-Kettenis, 2013). It is recognized that GD is rarely if ever reported in conjunction with some DSDs, such as Turner's syndrome and complete androgen insensitivity syndrome, but that it is overrepresented relative to the general population in association with other DSDs, such as congenital adrenal hyperplasia (CAH) and partial androgen insensitivity syndrome (Dessens, Slijper, & Drop, 2005; Mazur, 2005; Mazur et al., 2007). Jordan-Young (2012) argued that the gender-atypical interests and attitudes of females with CAH plausibly reflect a complex set of influences—the general physiological effects of adrenal androgens, the consequences of medical interventions and surveillance, the sexual effects of atypical genital morphology, and altered societal expectations—rather than simple masculinization of brain gender by elevated androgen levels. Similar considerations may be relevant to understanding the etiology of GD in other DSD syndromes as well.

Individuals with DSDs who experience GD typically identify as men or women of the gender other than their assigned gender, but some may identify as *intersex*, *intersexual*, or *epicene* persons (Bearman, 2007; Harper, 2007; Preves, 2003).

Subtypes of GD in Adults: Clinical Features

The *DSM-III* described transsexualism as a "heterogeneous disorder" (APA, 1980, p. 261), and subsequent research has confirmed the diversity of clinical presentations in adults with GD. Biologic sex and sexual orientation are two features that account for much of this diversity (Lawrence, 2010b). Adult males with GD are more variable in clinical presentation than adult females with these conditions. Adult males with GD or transsexualism whose sexual orientation is characterized by exclusive attraction to men are called *homosexual* (or *androphilic*) gender dysphoric males or MtF transsexuals, because they are homosexual relative to their biologic sex. These persons are typically dramatically different in clinical presentation from adult males with GD or transsexualism whose sexual orientation is characterized by attraction to women, to women and men, or to neither sex, who are called *nonhomosexual* gender dysphoric males or MtF transsexuals (Blanchard, 1985, 1989b; see also Lawrence, 2010b). In adult males with GD or transsexualism, homosexual and nonhomosexual subtypes appear to represent distinctly different clinical spectra (Whitam, 1987) and plausibly reflect entirely different etiologies (Freund, 1985; Smith, van Goozen, Kuiper, & Cohen-Kettenis, 2005b).

The great majority of adult females with GD or transsexualism are exclusively attracted to women and are called *homosexual* (or *gynephilic*) gender dysphoric females or FtM transsexuals. Although these gender dysphoric females differ in important ways from their nonhomosexual counterparts, the differences between subtypes based on sexual orientation in females with GD are less pronounced and less well documented than differences between subtypes based on sexual orientation in males with GD. Key features of these four typological categories are summarized in Table 16.1 and are described below.

Homosexual (Androphilic) Males With GD Males with GD who are exclusively sexually attracted to men were usually conspicuously feminine as children; many or most probably would have met diagnostic criteria for GD during childhood and adolescence. Homosexual gender dysphoric males are usually also extremely feminine as

Table 16.1
Subtypes of GD in Adults

Homosexual Males With GD (MtF)	Nonhomosexual Males With GD (MtF)
Attracted only to men	Attracted to women, women and men, or neither
Conspicuously feminine during childhood	Not conspicuously feminine during childhood
Rarely sexually aroused by cross-dressing	Usually sexually aroused by cross-dressing
Usually seek treatment in their 20s or early 30s	Usually seek treatment in their late 30s, 40s, 50s, or after
Homosexual Females With GD (FtM)	**Nonhomosexual Females With GD (FtM)**
Attracted only to women	Attracted to men or women and men
Usually conspicuously masculine during childhood	Usually less overtly masculine during childhood
Sexual attitudes are strongly male-typical	Sexual attitudes are less male-typical
Usually seek treatment in their 20s or early 30s	Usually seek treatment in their 20s or early 30s

adults (Blanchard, 1988; Whitam, 1987, 1997) and are more feminine in appearance than their nonhomosexual counterparts (Smith et al., 2005b). They rarely report any history of sexual arousal with cross-dressing (Blanchard, 1985, 1989b). Whitam (1987) observed that "in most societies these persons regard themselves as homosexuals and are regarded by more masculine homosexuals as a natural part of the homosexual world" (p. 177); clinicians may find it useful to adopt this perspective as well. If homosexual males with GD seek sex reassignment, they usually do so in their 20s or early 30s (Blanchard, Clemmensen, & Steiner, 1987; Smith et al., 2005b). In past decades, gender dysphoric males who underwent sex reassignment in the United States, Canada, and western European countries were homosexual (androphilic) in orientation; currently, most gender dysphoric males who undergo sex reassignment in these countries are nonhomosexual (Lawrence, 2010c).

Nonhomosexual Males With GD Most males with GD seen by clinicians in the United States and many Western countries are nonhomosexual in orientation. They may describe themselves as sexually attracted to women, to women and men, or to neither sex, but their primary sexual attraction is toward females. In most cases they also are (or at one time were) sexually attracted to the thought or image of themselves as females, a paraphilic sexual interest called *autogynephilia* ("love of oneself as a woman"; Blanchard, 1989a, 1989b). The most common manifestation of autogynephilia is erotic cross-dressing. Most nonhomosexual males with GD have a history of erotic cross-dressing or cross-gender fantasy (Blanchard, 1985; Lawrence, 2005), and sexual arousal with cross-gender fantasy has been observed to be extremely common, perhaps almost universal, among nonhomosexual gender dysphoric males (Blanchard, Racansky, & Steiner, 1986). Anatomically focused autogynephilia (i.e., sexual arousal to the idea of having female anatomic features, such as breasts or a vulva) is especially characteristic of gender dysphoric males who seek surgical sex reassignment (Blanchard, 1993c). It may be conceptually useful to think of nonhomosexual males with GD as heterosexual males with an unusual paraphilic sexual interest that makes them want to *become what they love* (Lawrence, 2007) by turning their bodies into facsimiles of the persons they find sexually desirable, women (Freund & Blanchard, 1993), although few would probably describe themselves in this way (Lawrence, 2013). Nonhomosexual males with GD often have other paraphilic sexual interests, especially sexual masochism (Bolin, 1988; Lawrence, 2013; Walworth, 1997). Some nonhomosexual males with GD develop a secondary sexual interest in men, because they are aroused by the idea of taking a woman's sexual role with a man, thereby having their "physical attractiveness as women validated by others" (Blanchard, 1989b, p. 622).

Nonhomosexual males with GD usually were not conspicuously feminine during childhood nor are they conspicuously so as adults (Blanchard, 1990; Whitam, 1997). Some report mild gender nonconformity during childhood (Buhrich & McConaghy, 1977) but less so than homosexual gender dysphoric males (Zucker et al., 2012). They are also less feminine in appearance than their homosexual counterparts (Smith et al., 2005b). In past decades, they typically sought sex reassignment in their mid-30s or later (Blanchard et al., 1987; Smith et al., 2005b) and not uncommonly in their 50s or 60s (Lawrence, 2003). More recently, however, gender dysphoric males of both the

nonhomosexual and homosexual subtypes appear to be seeking sex reassignment at younger ages (Zucker et al., 2012).

Homosexual and Nonhomosexual Females With GD There are also two subtypes of gender dysphoric females based on sexual orientation, but these are less dissimilar than the two male GD subtypes. Homosexual and nonhomosexual females with GD, for example, apply for sex reassignment at roughly similar ages (Smith et al., 2005b); but the two female GD subtypes also display some significant differences. Homosexual females with GD, who are exclusively sexually attracted to women, were invariably conspicuously masculine during childhood (Smith et al., 2005b); most probably would have met diagnostic criteria for GD during childhood and adolescence. Nonhomosexual females with GD, who are sexually attracted to men or both women and men, "may have been girls with neutral interests or with some tomboy characteristics" (Smith et al., 2005b, p. 159), but they were usually less conspicuously and pervasively masculine during childhood. The sexual attitudes of homosexual gender dysphoric females are male-typical in many respects: They display greater sexual than emotional jealousy and report more sexual partners, more interest in visual sexual stimuli, and greater desire for phalloplasty than their nonhomosexual counterparts (Chivers & Bailey, 2000). Nonhomosexual gender dysphoric females have sexual attitudes that are less male-typical (Chivers & Bailey, 2000). They are also more likely to have comorbid psychopathology (Smith et al., 2005b), for reasons that are not well understood. Sexual arousal to cross-dressing or cross-gender fantasy does not appear to be a significant factor in the development of nonhomosexual GD in females (Smith et al., 2005b). Nonhomosexual females with GD were once believed to be rare, but they now comprise roughly 10% to 20% of females with GD in northern European countries (Kreukels et al., 2012).

DIAGNOSTIC CONSIDERATIONS

Diagnosing GD

The defining diagnostic criterion of GD (APA, 2013) is a marked incongruence between gender identity ("experienced/expressed gender") and assigned sex, manifesting as some combination of discomfort with anatomic sex, desire for the anatomy of the other sex, desire to live or be treated as a member of the other sex, or perceived psychological similarity to the other sex. There is also a requirement of clinically significant distress or impairment in functioning.

Like past editions of the *DSM*, the *DSM-5* has one principal diagnosis—GD—and one or more residual diagnoses. The two residual diagnoses in the *DSM-5* are other specified GD and unspecified GD. Other Specified GD is used where symptoms of gender dysphoria are present and there is clinically significant distress or impairment but the full criteria are not met and the clinician wishes to state why the presentation does not meet full diagnostic criteria. Unspecified GD is the same as other specified GD except that the clinician does not wish to communicate a reason (APA, 2013).

Differential Diagnosis

Differential diagnostic considerations for the diagnosis of GD in adults include transvestic disorder; schizophrenia, bipolar disorder, and other psychotic conditions; dissociative identity disorder; some personality disorders (PDs); body dysmorphic disorder; and gender nonconformity.

Although transvestic disorder is one of the differential diagnoses for GD, the two conditions can and do co-occur (Blanchard, 2010). It is useful, in fact, to think of transvestic disorder and the nonhomosexual subtype of male GD as points on a spectrum of symptomatology, rather than as discrete entities (Lawrence, 2009b). In persons with transvestic disorder, the absence of a marked incongruence between gender identity and assigned sex would exclude the diagnosis of GD. Many cross-dressing men who meet diagnostic criteria for transvestic disorder, however, describe cross-gender identities of some strength (Docter, 1988), and some express a desire to use feminizing hormone therapy (Docter & Prince, 1997).

Patients with schizophrenia, bipolar disorder, and other psychotic disorders sometimes experience delusional beliefs of being or becoming the other sex (Habermeyer, Kamps, & Kawohl, 2003; Manderson & Kumar, 2001); treatment of the psychotic condition usually leads to resolution of this cross-gender identification, but GD and psychotic disorders do, on rare occasions, co-occur (Baltieri & De Andrade, 2009; Haberman, Hollingsworth, Falek, & Michael, 1975). Cross-gender ideation sometimes occurs in dissociative identity disorder (Modestin & Ebner, 1995; Saks, 1998); persons with GD display fewer dissociative symptoms than patients with dissociative disorders (Kersting et al., 2003) but more than nonclinical controls. Persons with antisocial PD have been reported to seek sex reassignment in the absence of GD (Laub & Fisk, 1974). Some theorists (e.g., Lothstein, 1984; Person & Ovesey, 1974) have proposed that the identity diffusion associated with borderline personality disturbances might manifest as GD, implying that borderline PD could be a possible differential diagnostic consideration. Wilkinson-Ryan and Westen (2000) found that patients with borderline PD were more conflicted or unsure about their gender identity than nonclinical controls, but Singh, McMain, and Zucker (2011) found no individuals meeting criteria for GD among 100 women diagnosed with borderline PD. Pfäfflin (2007) suggested that body dysmorphic disorder focused on the genitals could be mistaken for GD; the absence of a marked incongruence between gender identity and assigned sex would exclude the latter diagnosis (see also Phillips et al., 2010). Persons with gender nonconformity sometimes report significant cross-gender identification or a preference for the gender role of the other sex but may not experience enough distress or functional impairment to meet full diagnostic criteria for GD.

Comorbid Psychiatric Conditions and Dual Diagnoses

Estimates vary on the prevalence of comorbid psychiatric conditions in persons with GD. Most studies have been conducted in persons diagnosed with transsexualism. Cole, O'Boyle, Emory, and Meyer (1997) found that only 6% of MtF transsexuals and 4% of FtM transsexuals gave a history of treatment for another *DSM* diagnosis, excluding substance abuse and PDs. Prevalence estimates based on clinicians'

interviews and evaluations are generally higher, suggesting important method variance across studies.

Haraldsen and Dahl (2000) observed that 33% of a mixed group of MtF and FtM patients had another current *DSM* disorder, excluding PDs; the figure reported by Bodlund and Armelius (1994) was 44%. Hepp, Kraemer, Schnyder, Miller, and Delsignore (2005) found another current *DSM* disorder, again excluding PDs, in 40% of MtF and 36% of FtM transsexuals. De Cuypere, Jannes, and Rubens (1995), on the other hand, diagnosed such disorders in only 23% of MtF and 0% of FtM patients. In two recent studies, Hoshiai et al. (2010) reported a current prevalence of comorbid psychiatric disorders in 19% of MtF and 12% of FtM patients in Japan, and Heylens et al. (2014) reported current prevalence figures of 38% for MtFs and 37% for FtMs for comorbid conditions (excluding PDs) in patients from four European countries.

Reported lifetime prevalence figures for *DSM* disorders other than PDs in MtF transsexuals include 21% (Verschoor & Poortinga, 1988), 45% (De Cuypere et al., 1995), 80% (Hepp et al., 2005), and 68% (Heylens et al., 2014). In FtM transsexuals, reported lifetime prevalence figures for *DSM* disorders other than PDs include 33% (Verschoor & Poortinga, 1998), 39% (De Cuypere et al., 1995), 55% (Hepp et al., 2005), and 71% (Heylens et al., 2014). Most of these figures are consistent with those found in other clinical populations but exceed those of nonclinical populations. Affective and adjustment disorders are consistently among the most common of these comorbid conditions. In Japan, Hoshiai et al. (2010) found that a lifetime history of suicidal ideation and self-mutilation was high in both MtFs (76% and 31%, respectively) and FtMs (71% and 32%, respectively).

Comorbid substance abuse ("dual diagnosis") is often considered separately from other *DSM* disorders. Prevalence estimates for comorbid substance abuse among transsexuals cover a wide range. Verschoor and Poortinga (1988) reported a lifetime history of substance abuse in only 11% of MtF and 4% of FtM patients. Cole et al. (1997), Hepp et al. (2005), and De Cuypere et al. (1995) found higher lifetime prevalence figures: 29%, 50%, and 50%, respectively, in MtF transsexuals, and 26%, 36%, and 62%, respectively, in FtM transsexuals.

Reported prevalence data for comorbid PDs are generally more consistent: Observed prevalence figures in mixed groups of MtF and FtM transsexuals include 20% (Haraldsen & Dahl, 2000), 33% (Bodlund & Armelius, 1994), and 42% (Hepp et al., 2005). Miach, Berah, Butcher, and Rouse (2000) found PDs in 29% of MtF transsexuals, whereas De Cuypere et al. (1995) reported PDs in 23% of FtM patients but in 70% of MtF patients—the last figure a notable outlier. Heylens et al. (2014) recently reported much lower figures: 12% in MtF patients and 18% in FtM patients. The higher figures are similar to those seen in other clinical populations but exceed those of nonclinical populations. Heylens et al. (2014) found that the most prevalent PDs in their large European study were avoidant, schizoid, and borderline, with the Cluster C disorders most common overall.

When there is psychiatric comorbidity in patients with GD, how might this be best understood? There are at least four ways in which to formulate it: (1) It might be explained by the social stigma that results from the patient's non-normative gender identity (e.g., Clements-Nolle, Guzman, & Harris, 2008; Herbst et al., 2008; Koken, Bimbi, & Parsons, 2009; Melendez & Pinto, 2007); (2) it can be conceptualized as a causal factor in understanding the genesis of the GD (e.g., de Vries et al., 2010); (3) the

presence of such difficulties might be related to generic risk factors that operate in the individual and/or the family of origin (e.g., genetics, parental psychopathology, social and economic adversity, etc.); and (4) it could be argued that the inherent distress associated with a GD, even in the absence of social stigma, could lead to other psychiatric problems. Levine and Solomon (2009) provided a useful essay that can help clinicians sort out which of these factors might be operative in an individual case.

EPIDEMIOLOGY

Prevalence and Sex Ratio

Population-based treatment data from European countries provide the best estimates of the prevalence of GD and transsexualism in Western societies (Zucker & Lawrence, 2009). In Belgium, the prevalence of transsexualism, defined as having undergone sex reassignment, is 1:12,900 for adult males and 1:33,800 for adult females (De Cuypere et al., 2007). Data from the Netherlands are similar: 1:11,900 adult males and 1:30,400 adult females (Bakker, van Kesteren, Gooren, & Bezemer, 1993). Primary care physicians in Scotland reported a prevalence of GD, treated with cross-sex hormone therapy or sex reassignment surgery (SRS), of 1:12,800 in adult males patients and 1:52,100 in adult female patients (Wilson, Sharp, & Carr, 1999); the overall prevalence of GD, treated or untreated, was 1:7,400 in males and 1:31,200 in females. Based on New Zealand passport data, Veale (2008) reported somewhat higher rates: 1:3,630 in males and 1:22,714 in females. In most Western countries, MtF transsexualism is two or three times as prevalent as FtM transsexualism (Garrels et al., 2000; Landén, Wålinder, & Lundström, 1996).

There is evidence that treatment-based studies underestimate the true prevalence of GD. In a large, population-based survey of persons 15–70 years old, conducted in the Netherlands, Kuyper and Wijsen (2014) found that 1.1% of males and 0.8% of females reported an incongruent gender identity (stronger identification with the other sex than with one's assigned sex). Persons reporting an incongruent gender identity combined with both a dislike of their sexed body characteristics and the desire to change their bodies with hormonal or surgical treatment included 0.2% of the males and 0.05% of the females. These results suggest that GD may be more prevalent than is generally supposed, but they also demonstrate that, although an incongruent gender identity may be a cardinal symptom of GD, it does not necessarily imply the presence of significant dysphoria or the desire to undergo hormonal or surgical treatment.

There is also evidence that GD is becoming more prevalent. Studies conducted in Sweden in the 1960s reported a prevalence of transsexualism of 1:37,000 in adult males and 1:103,000 in adult females (Landén et al., 1996), or roughly one-third of current estimates from treatment-based studies. The observed increase in prevalence probably reflects a lower threshold at which individuals consider themselves to be appropriate candidates for sex reassignment.

Two recent surveys revealed that 2.7% and 2.8% of adult males reported having experienced sexual arousal in association with cross-dressing (Ahlers et al., 2011; Långström & Zucker, 2005). These results imply that autogynephilic cross-dressers are probably the most numerous transgender subgroup. Many of these individuals,

however, probably do not experience their gender identities as incongruent with their assigned sex and, therefore, would not meet diagnostic criteria for GD. Moreover, most probably do not experience sufficient distress or impairment to meet diagnostic criteria for either GD or transvestic disorder.

Age of Onset

Some persons with GD report that they were aware of their transgender feelings from their earliest memories. The cross-gender behaviors and interests of most homosexual males and females with GD and of some nonhomosexual females with GD were usually evident in early childhood. Nonhomosexual males with GD typically report that they experienced their first desire to be the other sex or to change sex in middle childhood but sometimes as late as adolescence or adulthood (Lawrence, 2005, 2013; Nieder et al., 2011; Zucker et al., 2012).

PSYCHOLOGICAL AND BIOLOGICAL ASSESSMENT

Psychological Assessment

Psychological assessment in known or suspected cases of GD involves determining the presence or absence of GD, evaluating the nature and severity of the GD, and assessment of comorbid psychopathology. In adults, GD is diagnosed primarily on the basis of self-report: "There are no so-called objective tests, either medical or psychological, that serve as proof of the diagnosis" (Pfäfflin, 2007, p. 176). The clinician should obtain information about the client's psychosexual development, gender identification, sexual orientation, and feelings concerning sexed body characteristics and assigned gender role. Clients sometimes deliberately or inadvertently provide misleading information to caregivers, especially if they are eager to be approved for treatment (Walworth, 1997). Clinicians should not uncritically accept self-reported sexual orientation in male patients with known or suspected GD who have a history of sexual attraction to women: Many such patients develop secondary sexual attraction to men in connection with their cross-gender identification and inaccurately describe themselves as exclusively attracted to men, whereas experienced clinicians often judge otherwise (Nieder et al., 2011).

Questionnaires and scales for the objective assessment of GD exist but are not yet widely used in clinical practice. The gender-related scales of the Minnesota Multiphasic Personality Inventory–2 (*Mf*, *GM*, and *GF*; Butcher et al., 2001; Martin & Finn, 2010) provide objective measures of clients' gender-typical or atypical attitudes and interests (see, e.g., Gómez-Gil, Vidal-Hagemeijer, & Salmero, 2008). The Feminine Gender Identity Scale for Males (Freund, Langevin, Satterberg, & Steiner, 1977) and Masculine Gender Identity Scale for Females (Blanchard & Freund, 1983) have rarely been used outside of research settings. The Utrecht GD Scale (Cohen-Kettenis & van Goozen, 1997; see also Cohen-Kettenis & Pfäfflin, 2010) unfortunately has not yet been published in English. The Gender Identity/GD Questionnaire for Adolescents and Adults (Deogracias et al., 2007) is a recently developed, published instrument with good sensitivity and specificity; it has been cross-validated (Singh et al., 2010) and seems destined to achieve widespread acceptance.

The specific focus of GD can vary considerably among clients. GD may involve dissatisfaction with sexed body characteristics, gender role, or both; the specific pattern may affect treatment planning. Intensity of GD not only varies among clients but can also vary over time in the same client. GD often intensifies following significant crises or losses (Levine, 1993; Lothstein, 1979; Roback, Fellemann, & Abramowitz, 1984) but may moderate or remit when these have been resolved.

As noted previously, comorbid mental health problems are prevalent in persons with GD. Treatment of comorbid psychotic, affective, and anxiety disorders may be required before GD can be confidently diagnosed and adequately characterized. Any comorbid mental health problems must be reasonably well controlled as a precondition for approval for genital SRS (WPATH, 2011).

Biological Assessment

Physical examination and laboratory testing are of limited value in the assessment of GD. Physical examination could help ascertain the presence or absence of a DSD, which might lead to an assignment of a specifier in the former case. Some gender identity clinics routinely perform karyotyping in GD evaluations, but the procedure is expensive and the results will be normal in roughly 97% of patients with known or suspected GD or transsexualism (Auer, Fuss, Stalla, & Athanasoulia, 2013; Bearman, 2007; Inoubli et al., 2011). Nonautosomal positive findings in males will usually represent Kleinfelter syndrome (47, XXY) or an XYY karyotype (Auer et al., 2013; Buhrich, Barr, & Lam-Po-Tang, 1978; Snaith, Penhale, & Horsfield, 1991; Taneja, Ammini, Mohapatra, Saxena, & Kucheria, 1992; Wylie & Steward, 2008; see also Mouaffak, Gallarda, Baup, Olié, & Klebs, 2007). Bearman suggested that, if karyotyping is performed at all, it should be offered only to male patients with hypogonadism, tall stature, gynecomastia, or learning disorders. There are a few case reports in the literature showing sex chromosome abnormalities in FtM patients (Auer et al., 2013; Khandelwal, Aggarwal, & Jiloha, 2010; Turan et al., 2000).

Over the years, evidence for an elevated prevalence of polycystic ovary syndrome (PCOS) in female GD and transsexualism has been inconsistent. Baba et al. (2007) reported an unexpectedly high figure, 58%, in a Japanese sample; the same investigators subsequently reported a figure of 32% in FtM transsexuals who had never used testosterone (Baba et al., 2011). In contrast, a well-controlled study that used a rigorous definition of PCOS found a prevalence of only 11.5% in Dutch FtM transsexuals, not significantly different from the 9.6% found in healthy controls (Mueller et al., 2008). Because PCOS may be related to both prenatal and postnatal androgen levels, it would probably be useful for it to be ruled out as part of routine endocrinological evaluation.

CLINICAL COURSE, PROGNOSIS, AND TREATMENT

Clinical Course

The clinical course of GD is variable, not easily predictable, and not well understood, even in persons who have been carefully evaluated and diagnosed (WPATH, 2011). There are at least four recognized outcomes of severe GD (Carroll, 1999): (1) unresolved

or unknown, (2) acceptance of natal gender, (3) part-time cross-gender expression, and (4) full-time cross-living and sex reassignment.

Unresolved or Unknown Outcomes As many as half of clients who undergo evaluation or psychotherapy for GD may withdraw from treatment (Carroll, 1999). They may find the process prohibitively expensive, become impatient with a prolonged evaluation process, or feel ambivalent or hopeless about achieving a satisfactory solution to their gender concerns. Some clients who drop out subsequently resume treatment, but otherwise little is known about the natural history of GD in these individuals.

Acceptance of Natal Gender Acceptance of natal gender was once considered the optimal outcome for patients with GD. There have been no convincing demonstrations, however, that any form of psychiatric treatment can eliminate GD or facilitate acceptance of natal gender in adults who experience it; however, some adults with GD do appear to accept their natal gender (Marks, Green, & Mataix-Cols, 2000; Shore, 1984). Acceptance of natal gender sometimes occurs in persons who undergo treatment of comorbid psychological problems, are unwilling to risk losing their employment or their families, hold religious beliefs that condemn sex reassignment, or have physical characteristics that make it impossible for them to pass convincingly as members of the other sex (Carroll, 1999; Shore, 1984). Nonhomosexual men with GD sometimes successfully postpone treatment until they have completed parental or spousal obligations (Blanchard, 1994). The Standards of Care (WPATH, 2011) suggest various "options for social support and changes in gender expression" for individuals who decide not to live part- or full-time in a cross-gender role.

Part-Time Cross-Gender Behavior Persons with GD may decide to live part-time in their preferred gender role and part-time as members of their natal sex. They sometimes use masculinizing or feminizing hormone therapy or undergo surgical procedures to facilitate this process. Docter and Prince (1997) surveyed more than 1,000 heterosexual cross-dressers, none of whom lived full-time as women, and found that 17% would seek sex reassignment if possible, 28% considered their feminine self their preferred gender identity, and nearly 50% were either using feminizing hormones or wanted to do so. Many of these persons presumably experienced some degree of GD, yet decided to live only part-time as women. Adult females with GD sometimes live part-time in the cross-sex gender role as well, but this rarely becomes a focus of clinical attention and has not been as thoroughly documented.

Full-Time Cross-Living and Sex Reassignment Many clients with a presenting complaint of GD or transsexualism will want to undergo sex reassignment and live full-time as members of the other sex. In reality, full-time and part-time cross-gender behavior do not represent distinctly demarcated outcomes but rather points on a spectrum of options available to persons with GD, involving many possible choices of presentation, cross-gender role assumption, and anatomic modification. Some persons who live full-time in the cross-gender role do not undergo SRS and may not use cross-sex hormone therapy. Some persons who use cross-sex hormones and undergo SRS do not present themselves unambiguously as members of the other sex, but as gender-ambiguous, androgynous, or visibly transgendered individuals.

The decision to undertake full-time cross-living and sex reassignment and the process of actualizing this decision typically occurs in stages, similar to the stages of coming out for lesbians and gay men. Several multistage models of transsexual coming out have been proposed (e.g., Devor, 2004; Gagne, Tewksbury, & McGaughey, 1997; Lewins, 1995). These typically involve acknowledging GD, questioning and information gathering, developing a cross-gender identity, disclosing one's situation to significant others, cross-living, undergoing surgical sex reassignment if desired, and experiencing further evolution of gender identity after transition (Devor, 2004).

TREATMENT

Standards of Care for Persons With GD The WPATH, formerly the Harry Benjamin International Gender Dysphoria Association, promulgates Standards of Care (SOC) for the treatment of persons with GD and related conditions. The SOC are updated regularly, most recently in 2011 (WPATH, 2011). Historically, the SOC have reflected the consensus opinions of experienced professionals but rarely a higher quality of empirical evidence (Cohen-Kettenis & Gooren, 1999); accumulating empirical support for recommendations was one emphasis of the 2011 revision. The SOC are an important resource for treatment of persons with GD, even though some affected persons contest them (see Green, 2008).

The SOC describe four main treatment modalities for GD and transsexualism: psychotherapy, cross-sex hormone therapy, real-life experience in the desired gender role, and sex reassignment surgery (SRS)—a term that usually denotes feminizing genitoplasty in MtF transsexuals but can denote either mastectomy with chest reconstruction or masculinizing genitoplasty in FtM transsexuals. Not all patients with GD desire all these therapeutic modalities. Some patients, for example, are satisfied with cross-sex hormone therapy and full-time or part-time cross-living. The SOC state that hormone therapy, the real-life experience, and nongenital surgery can be provided separately or in any combination, but that feminizing or masculinizing genitoplasty should ordinarily be provided only to patients who have previously used cross-sex hormone therapy for at least one year and have successfully completed a minimum of 1-year, full-time real-life experience in the desired gender role (WPATH, 2011).

Psychotherapy Individual psychotherapy is not required by the SOC but is strongly encouraged (WPATH, 2011; see also Bockting, 2008). Psychotherapy is not intended to cure GD but to allow the client to explore his or her evolving gender identity, discuss relationship and employment issues, and consider treatment options. Seikowski (2007) argued that psychotherapy was most appropriate for patients with some type of personality disorder, but was not necessary for the majority. Persons with GD can also benefit from group psychotherapy (Stermac, Blanchard, Clemmensen, & Dickey, 1991), which can reduce feelings of isolation and provide opportunities to receive and give support, including advice about grooming and social presentation.

Cross-Sex Hormone Therapy Cross-sex hormone therapy suppresses or minimizes the secondary sex characteristics of a person's natal sex and promotes the development of

the secondary sex characteristics of the other sex. Recent review articles and expert guidelines describe the management of cross-sex hormone therapy (e.g., Gooren & Delemarre-van de Waal, 2007; Hembree et al., 2009). The SOC (WPATH, 2011) discuss eligibility criteria for cross-sex hormone therapy. Hormone therapy is usually prescribed for persons with GD who seek sex reassignment, but it also can be prescribed for those who do not wish to live full-time in a cross-gender role or who do not desire SRS.

Hormone therapy for males with GD and MtF transsexuals usually involves a combination of estrogens and antiandrogens. This feminizing hormone therapy typically results in breast growth, decreased muscle mass, reduction in the growth of facial and body hair, slowing of scalp hair loss, and decreased sexual interest. MtF transsexuals who receive treatment with feminizing hormone therapy display better psychological adjustment than their untreated MtF counterparts (Leavitt, Berger, Hoeppner, & Northrop, 1980) and report less anxiety and depression as well (Gómez-Gil et al., 2012).

Although feminizing hormone therapy is reasonably safe, one long-term follow-up study (Wierckx et al., 2012) found that 12% of hormone-treated MtF transsexuals experienced thromboembolic events (6%) or other significant cardiovascular problems (6%), and about one quarter displayed significant osteoporosis. Moreover, Asscheman et al. (2011) found that all-cause mortality in hormone-treated MtF transsexuals was 51% higher than in the general population, with most of the increase attributable to suicide, AIDS, cardiovascular disease, and drug abuse.

Hormone therapy for females with GD and FtM transsexuals usually involves only testosterone. This masculinizing hormone therapy causes increased facial and body hair, increased muscle mass, male pattern scalp hair loss, deepening of the voice, clitoral enlargement, and suppression of menses. Masculinizing hormone therapy also has emotional and psychological effects, including increased aggressiveness and anger-proneness and greater sexual interest and arousal (Costantino et al., 2013; Van Goozen, Cohen-Kettenis, Gooren, Frijda, & Van de Poll, 1995). Gómez-Gil et al. (2012) reported that FtM transsexuals who were receiving testosterone therapy reported less anxiety and depression than their counterparts who had not yet begun treatment. Asscheman et al. (2011) found that mortality in hormone-treated FtM transsexuals was no higher than in the general population.

Real-Life Experience in the Desired Gender Role Real-life experience in the desired gender role helps clients decide whether cross-living offers a better quality of life. Clients can undertake a real-life experience without professional help, and some clients will already be living full-time in a cross-gender role when clinicians first see them. It is not always easy to decide, however, whether clients are living full-time in their desired gender roles, especially given that the SOC do not require clients to live as typical members of the other sex, but merely to live in whatever gender role is congruent with their gender identity (WPATH, 2011).

Being regarded as a member of one's preferred sex during the real-life experience is usually easier for FtM than MtF transsexuals. Attribution of male status results from observed signs of masculinization, whereas attribution of female status occurs by a process of exclusion, when few or no signs of masculinization are observed (Kessler & McKenna, 1978). Although it is almost impossible for either MtF or FtM transsexuals to

remove all physical signs of their natal sex, residual signs of maleness in MtF transsexuals will often prevent their being regarded as unequivocally female, whereas residual signs of femaleness in FtM transsexuals will rarely prevent their being regarded as unequivocally male.

The SOC describe the real-life experience as a reversible step that, if successfully completed, allows clients and caregivers to consider the irreversible step of genital SRS with greater confidence (WPATH, 2011). In practice, however, the real-life experience may have irreversible social and economic consequences of its own, which clients may consider more serious than the potential consequences of genital surgery. The SOC also do not specify what a successful real-life experience should look like. Improvement in social and psychological functioning in the desired gender role is one possible measure of success, but such improvement can be difficult to demonstrate if negative social and economic consequences of prejudice and discrimination overshadow the psychological benefits of living in the desired gender role (Levy, Crown, & Reid, 2003).

Sex Reassignment Surgery

Feminizing Genitoplasty in Males With GD. Genital SRS for males with GD yields excellent cosmetic and functional results and a high degree of patient satisfaction (Gijs & Brewaeys, 2007; Giraldo, Mora, Solano, Gonzáles, & Smith-Fernández, 2002). All elements of MtF sex reassignment provide relief of GD (Kuiper & Cohen-Kettenis, 1988), but genital SRS offers particular social and psychological benefits. In a prospective controlled study of MtF SRS outcomes, patients who received expedited SRS reported better psychosocial outcomes than did waitlist controls (Mate-Kole, Freschi, & Robin, 1990). Good surgical results and absence of complications are associated with greater subjective satisfaction and better psychosocial outcomes (Lawrence, 2003; Ross & Need, 1989; Schroder & Carroll, 1999).

Reduction Mammaplasty and Chest Reconstruction in Females With GD. This is the surgical procedure that females with GD most frequently undergo and is arguably the most important one (Monstrey, Ceulemans, & Hoebeke, 2007). It is often performed early in the sex reassignment process, which the SOC explicitly allow.

Masculinizing Genitoplasty in Females With GD. There are no entirely satisfactory genital SRS techniques available to females with GD, and some forego this procedure entirely. Two genital SRS techniques have been most widely utilized in females with GD. In *metoidioplasty*, the hypertrophied clitoris is used to create a microphallus; in *phalloplasty* techniques, skin flaps or free skin grafts are used to create a neophallus that usually allows standing urination (Monstrey et al., 2007). Often the labia majora are fused to create a neoscrotum and testicular prostheses are inserted. An erection prosthesis can be inserted into the neophallus if desired. Complications related to graft/flap necrosis, urinary leakage or obstruction, and erection prosthesis problems are common following phalloplasty. These difficulties notwithstanding, the great majority FtM transsexuals who undergo phalloplasty report being satisfied with the results (Wierckx et al., 2011).

Results of Sex Reassignment Most studies of the outcomes of the sex reassignment process have involved MtF transsexuals who have undergone genital SRS, or FtM transsexuals who have undergone chest reconstruction. Nearly all such studies have concluded that sex reassignment generally, and SRS specifically, results in substantial relief of GD, high levels of patient satisfaction, favorable (or at least not worsened)

psychosocial outcomes, and a low prevalence of regret (Gijs & Brewaeys, 2007; Green & Fleming, 1990; Lawrence, 2003; Murad et al., 2010).

Factors associated with favorable outcomes of SRS include careful diagnostic screening of candidates, availability of social support, psychological stability, and freedom from surgical complications. Some studies have found that nonhomosexual MtF transsexuals are more likely to experience regret after SRS than their homosexual counterparts (Blanchard, Steiner, Clemmensen, & Dickey, 1989; Smith, van Goozen, Kuiper, & Cohen-Kettenis, 2005a), but one large study did not confirm this impression (Lawrence, 2003).

Although its outcomes are positive overall, SRS does not offer a solution to all the problems that persons with GD face. For example, Dhejne et al. (2011) found that Swedish transsexuals who had successfully completed SRS displayed higher mortality rates than age-matched controls of either sex, especially involving deaths from suicide; they were also at higher risk for suicide attempts and inpatient psychiatric hospitalization.

ETIOLOGICAL CONSIDERATIONS

It is important to recognize the limitations of theories and research findings relevant to understanding the etiology of GD and transexualism in adults. Much of the relevant research has addressed the etiology of GD as it manifests in children (for a review, see Zucker & Bradley, 1995), but most cases of GD in childhood remit before adulthood (Drummond, Bradley, Badali-Peterson, & Zucker, 2008; Green, 1987; Singh, 2012; Wallien & Cohen-Kettenis, 2008). There is even a recent study that showed that some children who had transitioned socially to live as members of the other gender "reverted" to living in the gender role that matched their natal sex (Steensma, Biemond, de Boer, & Cohen-Kettenis, 2010). Moreover, most research has been conducted in males with GD; females with GD have received less attention. In addition, theorists and researchers often have not distinguished between homosexual and nonhomosexual transsexual subtypes, even though these may have different etiologies.

Behavioral Genetics and Molecular Genetics

Behavioral Genetics Studies of the co-occurrence of behavioral traits within families and especially within monozygotic (MZ) twin pairs are the usual methods of estimating the influence of genetic factors on behavioral traits, including GD and gender nonconformity. Heylens et al. (2012) conducted an analysis of MZ and dizygotic (DZ) twin pairs in which one twin had been diagnosed with GID, including several previously unpublished pairs: Among 23 pairs of MZ twins, 9 pairs (39%) were concordant for GID, whereas among 21 pairs of same-sex DZ twins, none were concordant for GID, a statistically significant difference. There have also been two large studies of co-occurring transsexualism or related conditions in first-degree relatives of persons with transsexualism. Green (2000) reported 10 instances of co-occurring transsexualism or transvestism in the siblings, parents, or children of roughly 1,500 transsexual probands. Gómez-Gil et al. (2010) reported finding 12 pairs of non-twin siblings among a sample of 995 consecutive transsexual probands; the

prevalence of transsexualism in siblings of transsexuals, 1 in 211, was much higher than the estimated prevalence in the general population.

Coolidge, Thede, and Young (2002) conducted the best-known investigation of the heritability of GID in children. They studied 96 MZ and 61 dizygotic twin pairs, ages 4 to 17 years. They assessed GID using a six-item scale based on the *DSM-IV* criteria for GID, but none of the twins had been diagnosed clinically with GID. Coolidge et al. found that heritability accounted for 62% of the variance in GID scores and nonshared environment accounted for 38%. The prevalence of GID in the children was 2.3%, however, suggesting that the authors' threshold for ascertaining the condition was too low: Their conclusions about heritability arguably addressed childhood gender nonconformity rather than true GID. Two other studies that explicitly addressed the heritability of childhood gender nonconformity reached different conclusions, perhaps because of their different methodology: Bailey, Dunne, and Martin (2000) found that heritability accounted for 50% of variance in recalled childhood gender nonconformity among men and 37% among women, with nonshared environment accounting for the rest. Knafo, Iervolino, and Plomin (2005) found that heritability accounted for about 27% of variance in parent-reported gender atypicality in boys ages 3 to 4, with shared environment accounting for about 57% and nonshared environment accounting for 16%; the comparable figures for girls were heritability 42%, shared environment 43%, and nonshared environment 15%. Although childhood gender atypicality usually does not lead to GD in adulthood, it is one of the usual antecedents of the homosexual form of GD in both males and females, and it appears to be at least partly heritable, based on these studies.

Molecular Genetics Sexual differentiation of the mammalian brain is influenced by prenatal sex hormone activity (Garcia-Falgueras & Swaab, 2010; Gooren, 2006; Sánchez, Bocklandt, & Vilain, 2009; Savic, Garcia-Falgueras, & Swaab, 2010; Swaab, 2004). Consequently, researchers have hypothesized that abnormalities in genes that code for sex hormone receptors or for enzymes that catalyze the synthesis or metabolism of sex hormones might show associations with GID/transsexualism. Candidate genes include those coding for the androgen receptor (AR), estrogen receptor alpha (ERα), estrogen receptor beta (ERβ), and progesterone receptor (PR), and for the enzymes aromatase (CYP19), 17-alpha-hydroxylase (CYP17), and 5-alpha-reductase, type II (SRD5A2). Most studies have investigated differences between transsexual patients and same-sex controls in mean repeat numbers of specific polymorphisms in candidate genes or in the frequencies of specific mutant alleles or genotypes. None have attempted to differentiate between transsexual subtypes.

Henningsson et al. (2005) found no significant differences between MtF transsexuals and male controls for the AR or CYP19 genes, but they did find a significant difference for the ERβ gene. Hare et al. (2009) examined the same three candidate genes in MtF transsexuals and male controls, but they obtained different results: No significant differences for the CYP19 or ERβ genes, but a significant difference for the AR gene, albeit using a one-tailed test (a two-tailed test would have been nonsignificant); moreover, the false-positive rate among the controls was substantial. Bentz et al. (2007) reported no differences between MtF transsexuals and male controls or FtM transsexuals and female controls for the SRD5A2 gene. Bentz et al. (2008) found no differences between MtF transsexuals and male controls for CPY17 alleles and

genotypes, but they did find a significant difference in the case of FtM transsexuals and female controls. Ujike et al. (2009) detected no significant differences between MtF transsexuals and male controls or FtM transsexuals and female controls for the AR, ERα, ERβ, PR, or CYP19 genes. In a recent study of young MtF transsexuals, Lombardo et al. (2013) found no significant associated molecular mutations in candidate genes related to male sexual differentiation (AR, DAX1, SOX9, SRY, and the AZF region of Y).

In summary, there is little or no evidence at present that abnormalities related to molecular genetics account for GD or transsexualism: Most investigations have yielded negative results, and the few positive results have not been replicated by other investigators.

Neuroanatomy and Neurobiology

Neuroanatomy The central subdivision of the bed nucleus of the stria terminalis (BSTc), a hypothalamic or limbic nucleus, is sexually dimorphic: It is significantly larger and contains a larger number of neurons in men than in women. Zhou, Hofman, Gooren, and Swaab (1995) conducted a postmortem study of six MtF transsexuals and found that mean BSTc size was small and female-typical, a sex-reversed pattern. The MtF transsexuals supposedly included both homosexual and nonhomosexual types. Kruijver et al. (2000) studied the same six MtF transsexuals and found that mean neuron number in the BSTc was also sex-reversed. Similar postmortem findings in a gender dysphoric man who had never received hormone therapy suggested that cross-sex hormone therapy could not account for the sex-reversed pattern. Kruijver et al. proposed that "transsexualism may reflect a form of brain hermaphroditism" (p. 2041).

The validity of this putative marker was challenged by the discovery that the BSTc does not become sexually dimorphic until adulthood, long after the symptoms of MtF transsexualism typically appear (Chung, de Vries, & Swaab, 2002). Magnetic resonance imaging (MRI) studies also demonstrated that hormone therapy in MtF transsexuals was associated with significant reductions in the volume of the brain globally and the hypothalamus particularly (Hulshoff Pol et al., 2006). Hulshoff Pol et al. conjectured that, in the Zhou/Kruijver studies, "the altered size of the bed nucleus of the stria terminalis could have been due to the exposure of cross-sex hormones in adult life" (p. S108). Also using MRI, Schiltz et al. (2007) found that male pedophiles, too, had a lower than expected BST volume; noting the similar findings in MtF transsexuals, they proposed that "these alterations may not be specific to pedophilia but may rather be a feature of sexual abnormalities in general" (p. 744). Additional information about the sexual orientation of the six Zhou/Kruijver MtF transsexuals, reported by Garcia-Falgueras and Swaab (2008), was consistent with the hypothesis that all were nonhomosexual. In summary, a sex-reversed BSTc size and neuron number may be a marker for paraphilic male sexuality or for only nonhomosexual MtF transsexualism, rather than for all types of MtF transsexualism. Alternatively, the BSTc findings may be attributable to the effects of transgender hormone therapy.

In a postmortem study of 12 MtF transsexuals, including the six Zhou/Kruijver subjects, Garcia-Falgueras and Swaab (2008) found that the volume and neuron number of another sexually dimorphic hypothalamic nucleus, INAH-3, was sex-

reversed (female-typical); probably 11 of the 12 MtF transsexuals were nonhomosexual. Garcia-Falgueras, Ligtenberg, Kruijver, and Swaab (2011) subsequently conducted a postmortem examination of the volume and neuron number of yet another sexually dimorphic hypothalamic nucleus, the intermediate nucleus of the preoptic area (INAH-1), in 10 of these same 12 MtF transsexuals; they discovered intermediate values that did not differ significantly from either male or female controls. Further research will be needed to confirm or disconfirm these findings and clarify their implications for understanding the etiology of GD.

Investigators have recently used neuroimaging techniques to conduct neuroanatomic studies of patients with GD prior to treatment with cross-sex hormone therapy. Luders et al. (2009) used MRI to compare regional gray matter volumes in 24 MtF transsexuals (18 nonhomosexual, 6 homosexual) and male and female controls; the pattern observed in the MtF subjects more closely matched the male controls. In a subsequent comparison of regional cerebral cortical thickness in the same 24 MtF transsexuals and a group of male controls, Luders et al. (2012) found several areas of greater cortical thickness in the transsexual participants; in this respect, they resembled nontranssexual women, in whom cortical thickness is greater than nontranssexual men. Rametti, Carrillo, Gómez-Gil, Junque, Zubiarre-Elorza, et al. (2011) employed an MRI technique called diffusion tensor imaging (DTI) to examine the directional organization of specific white matter regions in the brains of 18 homosexual MtF transsexuals in comparison to male and female control groups; they found that the MtF transsexuals were intermediate between the males and females on most measures for which a sex difference existed and differed significantly from both men and women. When the same research group conducted a parallel investigation in FtM transsexuals (Rametti, Carrillo, Gómez-Gil, Junque, Segovia, et al., 2011), the results were different: The FtM transsexuals more closely matched the male control group. Savic and Arver (2011) used MRI to measure regional gray and white matter volumes in 24 nonhomosexual MtF transsexuals and in male and female controls: For most measures, the MtF participants did not differ from the male controls but differed significantly from the female controls; yet on a few measures—thalamus and putamen volumes, for example—the MtFs differed from both control groups. Zubiaurre-Elorza et al. (2013) used MRI to examine cortical thickness and subcortical volumes in 24 FtM transsexuals and 18 MtF transsexuals (all homosexual) and in male and female controls. MtF participants were found to exhibit female-typical cortical thickness, exceeding that of control males in several regions; FtM participants were found to have male-typical right putamen volumes, exceeding those of control females. Cantor (2011) interpreted the Rametti, Carrillo, Gómez-Gil, Junque, Zubiarre-Elorza, et al. (2011) and Savic and Arver (2011) studies as demonstrating that homosexual MtF transsexuals display at least partly feminized neuroanatomic features in the brain, whereas nonhomosexual MtF transsexuals do not, but instead display neuroanatomic features typical of neither nontranssexual men nor women.

Neurophysiology A few investigators have used neuroimaging techniques or electroencephalography (EEG) to conduct neurophysiological studies of patients with GD prior to hormone therapy. Berglund, Lindström, Dhejne-Helmy, and Savic (2008) studied the effect of inhaling odorous steroid compounds on regional cerebral blood flow in the hypothalamus in 12 nonhomosexual MtF transsexuals and in male and

female controls, using positron emission tomography; the MtF transsexuals displayed a pattern of activation intermediate between the male and female controls, but closer to the latter. Gizewski et al. (2008) used functional MRI (fMRI) to study patterns of cerebral activation in response to visual erotic stimuli in 12 MtF transsexuals, 10 of whom were nonhomosexual, and in male and female control groups; they found that the activation pattern displayed by the transsexuals more closely matched that seen in the female controls. Schöning et al. (2010) utilized fMRI to examine cerebral activation patterns during a mental rotation task in 11 untreated MtF transsexuals—also11 hormone-treated MtF transsexuals—and male controls. All three groups activated the classical cerebral mental rotation network, but with some regional differences between the controls and the two MtF groups, which did not differ from each other. Flor-Henry (2010) conducted quantitative EEG source analyses in 14 untreated MtF transsexuals—two thirds of whom were nondextral—and male and female nondextral control groups; the pattern observed in the MtF group more closely matched the female controls, with increased fast frequency sources in the right hemisphere.

In a neurophysiological study of FtM transsexuals, Nawata et al. (2010) used single-photon emission computerized tomography to compare regional cerebral blood flow (rCBF) in 11 homosexual FtM patients and 9 heterosexual female controls; the FtM persons showed significantly decreased rCBF in the left anterior cingulate cortex and increased rCBF in the right insula, relative to controls.

The proximate causes of these neurophysiological findings are, at present, unknown, and their implications for understanding the etiology of GD remain to be determined.

Learning, Modeling, and Life Events

Early psychoanalytic theorists viewed parenting behavior as etiologically important in childhood GD. Stoller (1968, 1975) emphasized maternal parenting style: He believed that the mother's excessive closeness to her son ("blissful symbiosis"; Stoller, 1975, p. 37) was largely responsible for the development of transsexualism in boys, whereas the mother's inability to achieve emotional closeness with an "unfeminine" daughter contributed significantly to the development of transsexualism in girls. Moberly (1986), in contrast, believed that transsexualism reflected a "same-sex developmental deficit" (p. 205), in which the child's inability to identify with the same-sex parent led to a defensive opposite-sex identification.

Although these psychoanalytic formulations may now seem overly simplistic, parenting behavior may nevertheless be etiologically important. Zucker and Bradley (1995) observed that the mothers of boys with GID often have a history of significant psychopathology (see also Zucker et al., 2003), which is positively correlated with their reinforcement of feminine behaviors in their sons; the authors proposed that the mothers of boys who develop GID may be unwilling or unable to limit or discourage their sons' cross-gender behavior. Something similar may occur with girls with GID: Maternal psychopathology may again be associated with an inability to limit cross-gender expression (Zucker & Bradley, 1995). Consistent with these observations, Simon, Zsolt, Fogd, and Czobor (2011) reported that, compared with nonclinical control subjects, adult MtF and FtM transsexuals described their mothers as less caring and affective but more controlling. MtF transsexuals also described their mothers as

more unreliable and abusive yet less demanding; they described their fathers as less caring, reliable, and available.

COGNITIVE INFLUENCES

Cognitive factors appear to play a limited role in the etiology of GD in adults. Most relevant theory and research has focused on a few specific areas: childhood development of cognitive schemas concerning gender, cognitive comparisons of self and others during transgender coming out, and cognitive contributions to cross-gender identity formation in transvestism and nonhomosexual MtF transsexualism.

Children develop cognitive schemas concerning gender identity and gender stereotypes during early and middle childhood (Martin, Ruble, & Szkrybalo, 2002). Some children with GD develop gender schemas that include a cross-gender identity, but the reasons for this are unclear: Perhaps these children observe that their behaviors and interests conform to opposite-sex gender stereotypes and mislabel themselves accordingly (Zucker & Bradley, 1995). Although such a cognitive process could explain the mechanism of cross-gender identity formation in children with GD, it does not explain the origins of the sex-atypical behaviors and interests that are the putative objects of cognitive appraisal. Moreover, most children with GD do not go on to become adults with GD.

Cognitive comparisons of self and others concerning gender-related interests and behaviors is a recognized mechanism of identity formation and consolidation in the process of coming out for transsexuals and other transgender persons. Devor (2004) observed that transgender persons typically use "a number of techniques of identity comparison to try to determine if there is an identity in which they can comfortably live their lives in their originally assigned gender and sex" (pp. 50–51). They subsequently undertake a similar cognitive process as they try to find an authentic identity within the other gender.

Docter's (1988) theory of gender identity formation in transvestism and nonhomosexual MtF transsexualism stressed the importance of fully enacting the cross-gender role through complete cross-dressing and public presentation. Implicitly, this is a cognitive process, grounded in self-observation ("I dress and behave like a female; therefore I *am*, in some sense, female"). Docter described the process of reconciling core gender identity and the emergent cross-gender identity as an attempt to resolve cognitive dissonance. He observed that this process could lead to integration of the cross-gender identity into the existing male self-system (i.e., a revised cognitive schema) or reorganization of the self-system to give primacy to the cross-gender identity (i.e., an alternative cognitive schema).

Sex and Ethnicity Considerations As previously noted, biological sex is a key feature that explains much of the diversity in the GD. GD in adults is 2 to 3 times more common in males than in females, perhaps because autogynephilia accounts for many cases of GD in males, whereas the analogous paraphilia is probably rare in females (Lawrence, 2009a) and accounts for few, if any, cases of GD in females.

The clinical manifestations of GD differ substantially in males and females. Males with GD are diverse with respect to sexual orientation, age at clinical presentation, and congruence between physical appearance and desired gender role; females with GD

are more homogeneous with respect to these variables. Cross-sex hormone therapy is highly effective in masculinizing the appearance of FtM transsexuals but much less effective in feminizing the appearance of MtF transsexuals. Genital SRS techniques for MtF transsexuals are highly refined and generally yield excellent results, whereas many FtM transsexuals forego genital SRS altogether, for want of a surgical technique that is affordable, has a low rate of significant complications, and predictably yields high-quality results.

The role of ethnicity in accounting for the etiology and clinical manifestations of GD is incompletely understood, but there is a significant association between ethnicity and MtF transsexual typology across national cultures, and probably within national cultures. In Asian, Polynesian, and Latin American countries, most MtF transsexuals (or, at least, the cultural equivalents of MtF transsexuals) are homosexual in orientation (e.g., Bartlett & Vasey, 2006; Collumbien et al., 2009; Ellingson & Odo, 2008; Infante, Sosa-Rubi, & Cuadra, 2009; Johnson, 1997; Khan et al., 2009; Khan, Rehan, Qayyum, & Khan, 2008; Koon, 2002; Kulick, 1998; Nanda, 1994), whereas in the United States, Canada, and most western European countries, the majority of MtF transsexuals are currently nonhomosexual in orientation (for review, see Lawrence, 2010c). Societal individualism appears to mediate the relationship between ethnicity and MtF transsexual typology: Nonhomosexual MtF transsexuals are relatively more prevalent in more individualistic societies and less prevalent in less individualistic societies (Lawrence, 2010c). There is also evidence of a significant association between ethnicity and MtF transsexual typology within the United States. Hwahng and Nuttbrock (2007) reported that Black and Hispanic transgender and transsexual males in New York City were more likely than their White counterparts to be homosexual in orientation. In a subsequent, larger study of transgender and transsexual males in New York City, most of whom were Black or Hispanic, the correlation between nonhomosexual orientation and White ethnicity was 0.60 (Nuttbrock et al., 2011; see also Lawrence, 2010a). Similarly, Kellogg, Clements-Nolle, Dilley, Katz, and McFarland (2001) observed that, in a predominantly (71%) non-White sample of transgender and transsexual men in San Francisco, about 64% were probably homosexual in orientation, a much higher percentage than has typically been observed among predominantly White MtF transsexual samples in the United States (Lawrence, 2010c).

CASE STUDY

Case Identification and Presenting Complaints

Jordan is a 22-year-old natal (biological) female who was referred by her college counselor for an assessment regarding her strong feelings of GD. When not living on campus, Jordan resided with her parents and a younger sibling. Her parents were both professionals and worked full-time. Jordan reported that her parents had a "weird" relationship, that her mother had just had an affair, and that her parents might separate. On the WAIS-IV, Jordan obtained a Full-Scale IQ of 103 (average range).

History and Assessment

Jordan recalled a childhood in which she never felt like other girls. She related more comfortably with her male classmates and enjoyed a variety of stereotypical masculine

activities. In particular, she recalled a long-standing fascination with science fiction and, as an adolescent and young adult, would attend Star Trek conventions. She identified most closely with the character Spock (originally portrayed by Leonard Nimoy). Jordan recalled never liking to wear girl-typical clothes in childhood, but noted that her mother was a "feminist, " so this was not a source of strain between them. Although Jordan identified more with the boys, she wore her hair very long and so was never mistaken as a boy in her social environment. In childhood, Jordan recalled that she never voiced a desire to be a boy, but felt, in retrospect, that she did not "fit in" with the other girls in her neighborhood and at school. Jordan did not recall being teased as a youngster for her gender-related behavior, but she felt estranged and "alienated" from her peers.

As Jordan started to go through puberty, she began to develop a strong aversion to her female body characteristics. She did not like her monthly menstrual periods and was "horrified" as her breasts began to grow. At the time of assessment, Jordan's main request was to have a bilateral mastectomy. She was less interested in cross-sex hormone therapy and had not yet contemplated whether she wanted surgery to create a neophallus. In terms of Jordan's social appearance, she presented as an androgynous youth, with short hair and a casual clothing style (she cut her hair short after high school graduation, to which she wore a suit and tie). She concealed her large breasts with layers of T-shirts and a sweatshirt. The clinical impression was that Jordan would likely be perceived by naïve others to be male, based on her physical presentation and gender-ambiguous name.

During adolescence, Jordan reported long periods of depression. She engaged in frequent self-cutting of her wrists and the upper portion of her legs and had frequent suicidal ideation. In adolescence, Jordan became aware of sexual attraction directed toward other girls, and there was a period in which she secretly self-identified as a lesbian; however, until she attended college, Jordan had had no interpersonal sexual relationships. Jordan felt quite alienated from both boys and girls her age and considered herself to be a "loner." Her only solace was attending Star Trek conventions and conversing via the Internet with other Star Trek aficionados. By the time Jordan graduated from high school, she became increasingly aware that she did not "feel" like a female, and she began to read on the Internet about transsexualism and transgenderism. She commented during the assessment that "I think I meet the criteria for gender identity disorder." She was extremely subdued as she said this and cried. In college, Jordan's depression deepened, and she sought out counseling at the health center and eventually revealed her gender dysphoric feelings. In college, Jordan has had one long-term sexual relationship with a girl who self-identifies as heterosexual and whom Jordan stated "accepts me as a guy." They would kiss and Jordan would engage in manual-genital exploration with her partner, but she would not let her partner touch her ("I have 'no-touch zones,' which she accepts").

When asked about her own ideas about her gender identity development, Jordan commented that she never felt particularly close to either of her parents, but, if anything, she identified more with her father because they shared an interest in science. Jordan talked at length about how her mother always would "rant on and on" about the "objectification" of women and that her mother would leave the family room at home if Jordan's father was watching television in which "good-looking women with their breasts partially exposed" were present. Jordan said that her mother

found these portrayals of women to be "disgusting." Jordan recalled that "My mom always talked about women being the sex objects of men." Jordan recalled feeling ashamed of her own breast development, but that she could not talk about this with her mother as "My mom is sex phobic."

Based on the assessment, Jordan clearly met the *DSM-5* criteria for GD (Points A and B), She also met criteria for persistent depressive disorder (dysthymia). After the assessment, Jordan entered weekly psychotherapy for a year with a clinical psychology trainee who worked in a specialized gender identity service. Therapy focused on helping Jordan consolidate a male gender identity and role, gradually transitioning to living as a male. Jordan did not identify himself to others as transgendered, but as a "guy." Jordan's depression began to lift, and there was a marked diminution of suicidal ideation and self-cutting. Two years after the assessment, Jordan received a bilateral mastectomy and thereafter began a regimen of cross-sex hormone therapy. The major crisis during treatment was that Jordan's girlfriend ended their relationship, which resulted in a transient period of intense depression. In general, Jordan reports greater comfort with himself as a guy, although he struggles with the fact that "I have nothing between my legs." Nonetheless, Jordan feels that he will be able to establish new romantic partnerships with understanding heterosexual women.

SUMMARY

GD refers to severe discomfort with one's biological sex or assigned gender, reflecting a marked incongruence between one's gender identity and assigned sex. Biologic sex (male vs. female) and sexual orientation (homosexual vs. nonhomosexual) define four GD subtypes that differ in clinical presentation. Possible outcomes of GD include acceptance of assigned gender, part-time cross-gender expression, or sex reassignment and full-time cross-gender living. Individual and group psychotherapy can benefit some persons with GD. Treatment with cross-sex hormone therapy and SRS usually provides significant relief of GD, high levels of patient satisfaction, and favorable psychosocial outcomes.

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CHAPTER 17

Substance-Related Disorders: Alcohol

ERIC F. WAGNER, MICHELLE M. HOSPITAL, MARK B. SOBELL, and LINDA C. SOBELL

DESCRIPTION OF THE DISORDER

This chapter addresses diagnostic and assessment issues across the continuum of individuals suffering with alcohol problems, ranging from "misusers" to those who are severely dependent on alcohol. Although scientific study and clinical treatment historically focused on individuals who were severely dependent on alcohol, it is now widely recognized that such persons constitute a minority of the public suffering with alcohol problems. Epidemiological studies reveal that individuals with less serious alcohol problems outnumber those with severe alcoholism (Curry, Ludman, Grothaus, Gilmore, & Donovan, 2002; Institute of Medicine, 1990; World Health Organization, 2004). This recognition has led to increased research on and clinical attention to individuals with less severe alcohol problems, as well as the widespread acknowledgment that alcohol use problems lie along a continuum. To this end, changes in the alcohol use disorders diagnostic criteria from the fourth to the fifth editions of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*; American Psychiatric Association [APA], 2000a, 2013) reflect a move to a continuum-based (vs. taxonomy-based) conceptualization of alcohol use problems, and functionally extend the diagnosis to less severe cases.

In anticipation of publishing the *DSM-5*, the American Psychiatric Association convened a Substance-Related Work Group to update and improve the alcohol use disorder diagnostic criteria. The work group concluded that the overuse of the terms *addiction* and *dependence* has confused the diagnosis and treatment of people with alcohol use disorders and resulted in patients with normal tolerance and withdrawal being labeled as "addicts." Moreover, they agreed that alcohol use problems are best conceptualized as a unitary construct, a conceptual shift from the biaxial distinction between alcohol abuse and dependence that appeared in *DSM-IV*. In addition, the work group eliminated the *DSM-IV* legal problems criterion from the *DSM-5* criteria given substantial research documenting its limited clinical utility. They also added a new criterion to the *DSM-5,* alcohol craving, based on mounting empirical evidence in support of its diagnostic utility and centrality in regard to alcohol use disorder.

Several recent studies have supported the *DSM-5* changes in regard to alcohol use disorders, particularly the adoption of a one factor model of disorder (e.g., Hagman & Cohn, 2011; Kuerbis, Hagman, & Sacco, 2013; Mewton, Slade, McBride, Grove, &

Teesso, 2011). Interestingly, a recent study of the WHO's *ICD-10* alcohol dependence and harms criteria also supported a one-factor model. Thus, studies of both the American and international diagnostic systems' criteria for alcohol use disorders support a single factor conceptualization. Moreover, it appears that the *DSM-5* criteria are an improvement over the *DSM-IV* criteria for identifying those with low severity alcohol use disorders, particularly in college student (Hagman & Cohn, 2011) and older adult populations (Kuerbis, Hagman, & Sacco, 2013). That said, most studies have found only modest differences in alcohol use disorders prevalence rates when comparing the *DSM-IV* and *DSM-5* (e.g., Dawson, Goldstein, & Grant, 2013; Edwards, Gillespie, Aggen, & Kendler, 2013), a finding that led Dawson et al. (2013) to conclude "[o]n the whole, the similarities in profiles of DSM-IV and DSM-5 AUD far outweighed the differences" (p. E312).

In *DSM-5*, alcohol use disorder is defined as a problematic pattern of use leading to significant impairment or distress as manifested by at least two behaviors such as: (a) using alcohol in larger amounts or for a longer time than intended; (b) a persistent desire or unsuccessful attempts to cut down or control use; (c) significant time being spent to obtain, use, or recover from alcohol use; (d) cravings or strong desires (urges) to use; (e) failure to fulfill obligations; (f) interpersonal problems occur because of persistent use; (g) the individual gives up important activities (work, social interaction) because of alcohol; (h) evidence of tolerance (defined as the need for increasing amounts of alcohol to achieve intoxication or a markedly diminished effect with continued use of the same amount); and (i) withdrawal (defined as physiological responses that occur after consistent and excessive use).

In *DSM-5,* a diagnosis of alcohol use is given a severity rating. Mild alcohol use disorder is assigned when two or three of the previously mentioned behaviors are present; moderate severity is defined as the presence of four or five symptoms; and six or more symptoms is labeled severe.

Current views about alcohol use problems are a grafting of concepts derived from research, clinical anecdotes, and common wisdom. Over the past century, public opinion has softened from viewing those who suffer with alcohol problems as moral reprobates to being victims of a disease. In the United States, the view that alcohol problems are a medical disorder became dominant in the mid-1900s with the rise of Alcoholics Anonymous (AA), the seminal work of E. M. Jellinek, and the proclamation by the American Medical Association that alcoholism is a disease. The embracing of the disease concept was intended to shift responsibility for dealing with alcohol problems from the criminal justice system to the health-care system.

Alcoholics Anonymous, the ubiquitous mutual help approach that emerged in the 1930s, viewed alcoholism as a biological aberration—an "allergy" to alcohol (i.e., with repeated exposure to alcohol, alcoholics would quickly become physically dependent on the substance, and once dependent they would continue to drink to avoid withdrawal symptoms). To explain relapse, AA stated that alcoholics had an "obsession" to drink like normal drinkers. In addition, alcoholism was thought to be a progressive disorder (i.e., if alcoholics continued to drink, their problem would inevitably worsen), and persons who were mildly dependent on alcohol were thought to be in the "early stages" of developing alcoholism. Consequently, even those with mild problems were viewed as needing the same treatment as those who were severely dependent.

E. M. Jellinek, a scientist, attempted to bridge the gap between lay views and the evidence in support of the disease concept. He and others felt that the medical profession should be responsible for treating alcohol abusers (Bacon, 1973). Although he alluded to genetic components, he did not speculate as to why some drinkers develop alcohol problems but others do not. Jellinek did postulate that alcoholics: (a) use alcohol to cope with emotional problems; (b) over time develop tolerance to alcohol, thereby leading to increased consumption to achieve desired effects; and (c) eventually develop "loss of control," where even small amounts of alcohol would initiate physical dependence and trigger more drinking (Jellinek, 1960). Finally, Jellinek proposed that there were many types of alcohol problems, including gamma alcoholism, which he felt was the most common type in the United States and a progressive disorder.

Over the past half century, considerable research has refuted these traditional conceptualizations. Although some individuals may be genetically predisposed to develop alcohol problems, a large proportion of individuals with alcohol problems do not have this positive family history, and a large proportion of individuals with a positive family history for alcohol use disorders do not have alcohol problems (Dahl et al., 2005; Humphreys, 2009). Research shows that social and cultural factors play a large role in the development of alcohol problems (Hendershot, MacPherson, Myers, Carr, & Wall, 2005; Miles, Silberg, Pickens, & Eaves, 2005; Penninkilampi-Kerola, Kaprio, Moilanen, & Rose, 2005). Moreover, in most cases of alcohol problems, the natural history of the disorder is not progressive (Dawson, 1996; Institute of Medicine, 1990); rather, it includes periods of alcohol problems of varying severity separated by periods of either nondrinking or drinking limited quantities without problems (Cahalan, 1970; King & Tucker, 2000). Also, natural history studies have found that recovery from alcohol problems in the absence of treatment is more prevalent than once thought (Bischof, Rumpf, Hapke, Meyer, & John, 2003; Dawson et al., 2005; Klingemann et al., 2001; Klingemann, Sobell, & Sobell, 2009; Mohatt et al., 2007; Sobell, Cunningham, & Sobell, 1996; Sobell, Ellingstad, & Sobell, 2000).

With regard to loss of control, research has demonstrated that even in very severe cases, physical dependence is not initiated by a small amount of drinking (Marlatt, 1978; Pattison, Sobell, & Sobell, 1977); other factors, such as conditioned cues (Niaura et al., 1988) and positive consequences of drinking (Orford, 2001), are necessary to explain why some people continue drinking despite having repeatedly suffered adverse consequences (Humphreys, 2009). Finally, considerable research shows that mildly dependent alcohol abusers respond well to brief interventions, often by reducing their drinking to nonproblematic levels rather than ceasing their drinking (Bien, Miller, & Tonigan, 1993; Cunningham, Wild, Cordingley, van Mierlo, & Humphreys, 2010; Hester, Delaney, Campbell, & Handmaker, 2009; Sobell & Sobell, 1993; Sobell & Sobell, 1995).

CLINICAL PICTURE

Unless the reasons to stop drinking are extremely compelling, individuals with alcohol problems are very ambivalent about ending their alcohol use. Alcohol use is widespread in our society, and even those with severe alcohol dependence like the subjective experience of drinking. For individuals at the less severe end of the alcohol

problem continuum, ambivalence can be very pronounced because the decision to stop or reduce drinking is based on probable risks rather than certain consequences. Failure to recognize this commonplace and logical ambivalence about stopping drinking can seriously compromise the success of the assessment and treatment process.

Traditional conceptualizations assert that individuals with alcohol problems will present in denial; that is, they will fail to recognize that their drinking is a problem (Nowinski, Baker, & Carroll, 1992). In response, traditional interventions attempt to confront and break through the denial. The rationale is that this procedure is consistent with the first step of AA (i.e., recognizing that one is powerless over alcohol; Nowinski et al., 1992). However, being confronted and labeled as alcoholic often elicits resentment, retaliation, and resistance to intervention. Stated simply, a confrontational approach to assessment and treatment can cause otherwise receptive clients to deny that they have an alcohol problem. An alternative approach concentrates on the ambivalence and avoids the use of confrontation, labeling, or other tactics that provoke defensiveness and resistance. This alternative nonthreatening, nonconfrontational style of interviewing is called motivational interviewing (MI; Miller & Rollnick, 1991, 2002, 2013; Substance Abuse and Mental Health Services Administration, 1999), which has grown immensely in popularity over the past two decades. Several randomized controlled trials (RCTs) of brief interventions using MI principles have found clinical significant improvements among individuals with alcohol problems (Bien et al., 1993; Burke, Arkowitz, & Menchola, 2003; Copeland, Blow, & Barry, 2003; Heather, 1990; Rubak, Sandbæk, Lauritzen, & Christensen, 2004; Sobell & Sobell, 1993), which has led MI to becoming accepted as an empirically supported treatment approach for alcohol problems.

DIAGNOSTIC CONSIDERATIONS

Diagnostic formulations play an integral role in decisions about treatment goals and intensities, and are a requirement of insurance and clinical recording. An accurate diagnosis defines the problem in a way that can be communicated and understood by clinicians and researchers. A diagnostic formulation coupled with an assessment provides an initial understanding of the problem as well as a foundation for initial treatment planning. The two major diagnostic classifications of mental disorders are the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*) and the Mental Disorder section of the *International Classification of Diseases* (*ICD*). The first *DSM* (*DSM-I*) was published in 1952 by the American Psychiatric Association and was a variant of the *ICD-6*. Over the past few decades, changes in the *DSM* alcohol use disorder classification criteria have reflected both the state of knowledge and contemporary attitudes. For example, while the *DSM-III-R* viewed alcohol dependence as a graded phenomenon ranging from mild (enough consequences to meet criteria but no major withdrawal symptoms) to severe (several negative consequences and withdrawal symptoms), the *DSM-IV* separated psychological from physiological dependence by making physical dependence a specifier rather than a central symptom. Presently, the *DSM-5* eliminates the distinction between alcohol dependence and alcohol abuse, and instead views alcohol use disorders as varying only in terms of severity.

Several common clinical features of alcohol use disorders complicate their diagnosis and treatment. First, there is a high prevalence of co-occurring psychiatric disorders among individuals with alcohol problems (National Survey on Drug Use and Health [NSDUH], 2004, 2006, 2007; Nunes, Selzer, Levounis, & Davies, 2010). Psychiatric disorders with an exceptionally high co-occurrence with alcohol disorders include mood disorders such as depression, anxiety disorders, schizophrenia, and personality disorders such as antisocial personality disorder and borderline personality disorder. Given the frequent co-occurrence with psychiatric disorders, diagnostic formulation with alcohol disorders must assess three things: (1) the extent and nature of the alcohol problem; (2) the extent and nature of psychiatric disorders; and (3) and the extent and nature of interaction between alcohol problems and psychiatric problems (Boden & Moos, 2009; Mack, Harrington, & Frances, 2010). Ideally, individuals should be alcohol free for several weeks in order to accurately assess for co-occurring psychiatric diagnoses, because active alcohol use can mask or exacerbate psychiatric symptoms (Schuckit, 1995).

Several studies have shown that people with alcohol use problems with co-occurring psychiatric problems have poorer treatment outcomes than people with alcohol use problems without co-occurring psychiatric problems (Le Fauve et al., 2004; Nunes et al., 2010). Although an integrated treatment approach involving additional and specialized counseling is often suggested for clients who have co-occurring disorders (Steele & Rechberger, 2002), there is a lack of empirical data about whether ancillary counseling improves treatment outcomes among individuals with a dual diagnosis of alcohol and psychiatric disorders (Assanangkornchai & Srisurapanont, 2007; Baigent, 2005; Echeburúa, Bravo de Medina, & Aizpiri, 2007; Le Fauve et al., 2004; Trull, Jahng, Tomko, Wood, & Sher, 2010; Whicher & Abou-Saleh, 2009).

Second, many individuals with alcohol disorders also have problems with the use of other substances. For people with alcohol problems who use other drugs including nicotine, it is important to gather a comprehensive profile of all types of psychoactive substance use and substance use problems. Over the course of an intervention, drug use patterns may change (e.g., decreased alcohol use, increased smoking; decreased alcohol use, increased cannabis use). Furthermore, alcohol abusers who use other drugs may experience pharmacological synergism (i.e., a multiplicative effect of similarly acting drugs taken concurrently) and/or cross-tolerance (i.e., lessened drug effect because of past heavy use of pharmacologically similar drugs), both of which must be considered when treating those with alcohol problems who use other drugs. The foregoing speaks to important differences between the treatment of individuals with alcohol use problems only and of individuals who have other substance use problems in addition to their alcohol use problems (Batki et al., 2009; González-Pinto et al., 2010; Pakula, Macdonald, & Stockwell, 2009; Shillington & Clapp, 2006).

Third, people with an alcohol use disorder who drink alcohol daily and in large quantities are likely to experience withdrawal symptoms when access to alcohol is restricted. These symptoms can range from minor withdrawal symptoms (e.g., psychomotor agitation) to, in the most severe cases, delirium tremens (DTs). A history of past withdrawal symptoms, coupled with reports of recent heavy ethanol consumption, can alert clinicians that withdrawal symptoms are likely to occur upon cessation of drinking; such symptoms can be successfully managed with medical

interventions. Moreover, some research suggests that severity of alcohol dependence may interact with response to treatment goals; different treatment intensities may be the most appropriate treatment with different levels of dependence (e.g., mild vs. severe), consistent with client-treatment matching (Babor & Del Boca, 2003; McKay, 2009). Thus, important diagnostic goals when assessing individuals with alcohol problems are to determine the severity of the problem and whether withdrawal symptoms are likely to occur when drinking is reduced.

EPIDEMIOLOGY

Next to caffeine, alcohol is the second most used psychoactive substance (Adams, Martinez, & Vickerie, 2009). The World Health Organization (WHO, 2004) estimates that approximately 2 billion people worldwide consume alcoholic beverages and 76.3 million people have diagnosable alcohol use disorders. The global burden related to alcohol consumption, both in terms of (a) morbidity and mortality and (b) economic and social costs, is considerable. Worldwide, it has been estimated that alcohol causes 1.8 million deaths (3.2% of total) and a loss of 58.3 million (4% of total) of Disability-Adjusted Life Years (DALY) (WHO, 2004). High-level, long-term, chronic drinking dramatically increases the risk for more than 60 diseases (English & Holman, 1995; Gutjahr, Gmel, & Rehm, 2001; Ridolfo & Stevenson, 2001; Single, Robson, Rehm, & Xi, 1999). Alcohol use problems play a causal role in 20% to 30% of esophageal cancer, liver cancer, cirrhosis of the liver, homicide, epileptic seizures, and motor vehicle accidents worldwide (WHO, 2004). Acute intoxication from drinking is associated with motor vehicle traffic accidents, homicide and unintentional or intentional injury, falls, and poisonings (WHO, 2004). Moreover, alcohol consumption is linked to many harmful consequences for the individual drinker, the drinker's immediate environment, and society as a whole. Alcohol-related social consequences include traffic accidents, workplace-related problems, family and domestic problems, and interpersonal violence (Klingemann & Gmel, 2001).

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) surveyed a representative sample of 42,862 American adults in the National Longitudinal Alcohol Epidemiologic Survey (Grant, 1997). It was found that the lifetime prevalence of alcohol dependence was 13.3%, and the past-year prevalence was 4.4%. Men were more likely than women to use alcohol and to have alcohol use disorders. NIAAA conducted a second survey of a representative sample of 43,093 Americans in the National Epidemiologic Survey on Alcohol and Related Conditions (Stinson et al., 2005) and found the 12-month prevalence of alcohol use disorders to be only 7.35%, and of comorbid alcohol and substance use disorders to be 1.10%. In terms of the stability of diagnoses, Hasin, Grant, and Endicott (1990) found that of those individuals originally diagnosed as alcohol dependent, 46% were still classified as dependent 4 years later, 15% were classified as having alcohol abuse, and 39% could not be diagnosed with an alcohol problem. Similarly, in a national survey, Dawson (1996) found that among 4,585 adults who previously had met criteria for a *DSM-IV* diagnosis of alcohol dependence, 28% still met the criteria for alcohol abuse or dependence, 22% were abstinent, and 50% could not be diagnosed as having an alcohol problem. As compared to people who had not been in treatment, treated individuals were more likely to be abstinent (39% vs. 16%), whereas those who had not

been treated were more likely to be drinking asymptomatically (58% vs. 28%). In another national survey, Dawson (2000) reported that frequency of intoxication had the strongest association with the probability of having a diagnosable alcohol use disorder, followed by the frequency of drinking five drinks per day. These findings underscore that alcohol problems are not necessarily progressive.

From the standpoint of symptom-based prevalence, the ratio of problem drinkers to severely dependent drinkers is a function of the definitions used and the populations sampled. Regardless of the definitions, on a problem severity continuum the population of persons with identifiable problems but no severe signs of dependence is much larger than the population with severe dependence. Problem drinkers constitute 15% to 35% of individuals in the adult population, whereas severely dependent drinkers account for 3% to 7% (Hilton, 1991; Institute of Medicine, 1990). Moreover, the prevalence of alcohol abuse is approximately twice the prevalence of alcohol dependence (Harford, Grant, Yi, & Chen, 2005).

Drinking problems are not distributed equally across sociodemographic groups. Males continue to outnumber females (NIAAA, 2005), though the gender gap in alcohol use disorders has been narrowing since the Vietnam War (Grant, 1997). Besides gender differences in prevalence, problem drinking tends to occur later in life for women (NIAAA, 2005). Alcohol-related problems also appear to be inversely related to age, with the highest problem rates occurring for those 18 to 29 years of age (Fillmore, 1988; NIAAA, 2000; Robins & Regier, 1991; Substance Abuse and Mental Health Services Administration [SAMHSA], 2004). Marital status also is related to problem drinking, with single individuals experiencing more physiological symptoms of dependence and more psychosocial problems than those who are married (Hilton, 1991; SAMHSA, 2006). Specifically, alcohol abuse or dependence is more prevalent among adults who have never married (16.0%) than among adults who are divorced or separated (10.0%), married (4.6%), or widowed (1.3%) (SAMHSA, 2006).

Even though epidemiological studies provide information on ethnic and racial differences in relation to alcohol use and abuse, the methods used for categorizing respondents' cultural/ethnic backgrounds have been rudimentary. Consequently, data on ethnic differences must be considered preliminary. That said, across ethnic/racial groups, national epidemiological studies consistently document ethnic variation in drinking, alcohol use disorders, alcohol use, and treatment engagement and retention (Chartier & Caetano, 2010). Compared with other ethnic groups, (a) Native Americans and Hispanics report higher rates of high-risk drinking; (b) Native Americans and Whites have a greater risk for alcohol use disorders; (c) Native Americans, Hispanics, and Blacks experience more severe drinking-related consequences; and (d) Hispanic problem drinkers are less likely to enter and stay in treatment. Moreover, among alcohol-dependent drinkers, Blacks and Hispanics are more likely to demonstrate recurrent or persistent alcohol dependence. Among Asian Americans, alcohol problem rates are generally lower than among other ethnic and cultural groups (Galvan & Caetano, 2003; Makimoto, 1998; NIAAA, 1993). However, some evidence suggests that Asian Americans of mixed ethnic heritage may be at elevated risk for alcohol use problems (Price, Risk, Wong, & Klingle, 2002). Both Asian cultural norms and physiological sensitivity to alcohol appear to influence the likelihood of alcohol use problems among Asian American groups (Clark & Hesselbrock, 1988).

PSYCHOLOGICAL AND BIOLOGICAL ASSESSMENT

A thorough and careful assessment is critical to the development of meaningful treatment plans, and an accurate diagnosis of alcohol use and other concurrent disorders is integral to the assessment process. Assessment serves several critical functions; it provides clinicians with (a) an in-depth picture of a person's alcohol use, problem severity, and related consequences—this picture can be used to develop an individualized treatment plan tailored to the needs of each client; (b) an objective process by which to gauge treatment progress; and (c) empirical feedback about how a treatment plan already in place could be improved. The depth and intensity of an assessment will be related to problem severity, the complexity of the presenting case, and the specific interests of the clinician and/or researcher conducting the assessment. The instruments and methods described in this chapter can be used clinically to gather information that is relevant to the assessment and treatment planning process. The implications of assessment data for treatment issues, such as drinking goals and treatment intensity, show how the clinical interview can significantly affect treatment.

CRITICAL ISSUES IN ASSESSMENT

In the alcohol field, most research and clinical information is obtained through retrospective self-reports. Clients are asked to recount their use of alcohol and any alcohol-related negative consequences over a specified period or time, such as the past month, 90 days, or year. Research has confirmed that alcohol abusers' self-reports are generally accurate if clients are interviewed in clinical or research settings, when they are alcohol free (i.e., there is no alcohol in their system), and when they are given assurances of confidentiality. Self-reports are prone to some degree of inaccuracy, however, due to recall biases, social desirability biases, misinterpretation of questions, and the like. One way to confirm the accuracy of self-reports is to obtain overlapping information from sources such as chemical tests, collateral reports, and official records. Data from different sources are then compared and contrasted, and conclusions as to the presenting problems are based on a convergence of information. When the measures converge, one can have confidence in the accuracy of the reports.

Getting accurate information during the assessment of alcohol use problems is essential to the success of treatment. Information gathered through the assessment process can be used to provide feedback to clients to enhance their commitment to change. In order to make the assessment and feedback about the assessment most beneficial to clients, they should be delivered in a nonconfrontational manner using principles of motivational interviewing (Sobell & Sobell, 2008). Readers desiring a comprehensive description of how to do motivational interviewing and how to use advice/feedback from an assessment are referred to excellent publications by the Substance Abuse and Mental Health Services Administration (1999), the National Institute on Alcohol Abuse and Alcoholism (2005; Allen & Wilson, 2003), and the American Psychological Association (Sobell & Sobell, 2008).

With respect to the length of an assessment, the breadth and depth of an assessment for alcohol use disorders will vary due to heterogeneity in alcohol problem severity across clients. Because persons with less severe alcohol problems often respond well to a brief intervention, an assessment that is longer than the intervention makes little

sense (see Dunn et al., 2010). In contrast, severely dependent alcohol abusers may require a more intensive assessment covering such areas as organic brain dysfunction, psychiatric comorbidity, social needs, and medical status (e.g., liver function). Ultimately, an assessment should be based on clinical judgment and the client's needs. The next section describes different assessment areas and reviews relevant assessment instruments, scales, and questionnaires that can be used for assessing alcohol use and abuse. Only instruments that have sound psychometric properties and clinical utility are discussed. With respect to selecting an appropriate instrument for clinical or research purposes, it is helpful to ask, "What will I learn from using the instrument that I would not otherwise know from a routine clinical interview?"

Alcohol Use

Assessing alcohol consumption involves measuring the quantity and frequency of past and present use. When choosing an instrument to assess drinking, level of precision and time frame are key considerations. Two major dimensions along which measures differ are (1) whether they gather summarized information (e.g., "How many days per week on average do you drink any alcohol?") versus specific information (e.g., "How many drinks did you have on each day of the past month?") and (2) whether the information is recalled retrospectively or recorded in real time as it occurs. Specific measures are preferred over summary measures for pretreatment and within-treatment assessments because they provide (a) information about patterns of drinking and (b) opportunities to inquire about events associated with problem drinking that are not possible using summary data (e.g., "What was happening on Friday when you had 12 drinks?").

In terms of key instruments, there are four long-established approaches to assessing alcohol consumption: (1) lifetime drinking history (LDH; Skinner & Sheu, 1982; Sobell & Sobell, 1995; Sobell, Toneatto, & Sobell, 1994); (2) quantity-frequency methods (QF; Room, 1990; Skinner & Sheu, 1982; Sobell & Sobell, 1995); (3) timeline followback (TLFB; APA, 2000b; Sobell & Sobell, Sobell and Sobell, 1992, 1995, Sobell and Sobell, 2000); and (4) self-monitoring (SM; Sobell, Bogardis, Schuller, Leo, & Sobell, 1989; Sobell & Sobell, 1995). The first three are retrospective estimation methods (i.e., they obtain information about alcohol use after it has occurred). The TLFB can also be used in treatment as an advice-feedback tool to help increase clients' motivation to change (Sobell & Sobell, 1995). The fourth method, self-monitoring, asks clients to record their drinking at or about the same time that it occurred. The self-monitoring approach possesses several clinical advantages: (a) it provides feedback about treatment effectiveness; (b) it identifies situations that pose a high risk of relapse; and (c) it gives outpatient clients an opportunity to discuss their drinking that occurred since the previous session. Because several reviews have detailed the advantages and disadvantages of these drinking instruments, readers interested in the use of these instruments are referred to the primary source articles listed for each approach.

Alcohol Use Consequences

One of the key defining characteristics of a *DSM-5* diagnosis is alcohol-related consequences. Several short self-administered scales have been developed to assess

alcohol-related biopsychosocial consequences and symptoms: (1) Alcohol Use Disorders Identification Test (AUDIT; Saunders, Aasland, Babor, de la Fuente, & Grant, 1993); (2) Severity of Alcohol Dependence Questionnaire (SADQ; Stockwell, Murphy, & Hodgson, 1983; Stockwell, Sitharthan, McGrath, & Lang, 1994); (3) Alcohol Dependence Scale (ADS; Skinner & Allen, 1982); and (4) Short Alcohol Dependence Data Questionnaire (SADD; Raistrick, Dunbar, & Davidson, 1983). These scales take about 5 minutes to administer and range from 10 to 25 items in length. Given the elimination of the alcohol dependence diagnosis in the *DSM-5,* these "dependence" scales may well be in need of retitling. However, the types of symptoms these scales measure remain relevant for identifying people with alcohol use disorders of greater severity.

The AUDIT stands out for its psychometric characteristics, convenience, and cross-cultural validation. The AUDIT, developed as a multinational WHO project, is a brief screening test for the early detection of harmful and hazardous alcohol use in primary health care settings (Saunders et al., 1993). The 10 questions are scored based on the frequency of the experience (i.e., from 0 "never" to 4 "daily"). The AUDIT has been shown to be as good as or better than other screening tests (e.g., CAGE, MAST, ADS) in identifying individuals with probable alcohol problems (Barry & Fleming, 1993; Fleming, Barry, & MacDonald, 1991). According to the authors, the differences between the AUDIT and most other screening tests are that it (a) detects drinkers along the entire severity continuum from mild to severe (consistent with the *DSM-5*); (b) emphasizes hazardous consumption and frequency of intoxication compared with drinking behavior and adverse consequences; (c) uses a time frame that asks questions about current (i.e., past year) and lifetime use; and (d) avoids using a "yes/no" format and instead uses Likert rating scales to reduce face validity.

Co-Occurring Disorders

As reviewed earlier, a substantial number of people with alcohol problems have co-occurring psychiatric problems. Although several diagnostic interviews and scales exist for assessing psychiatric comorbidity among individuals with alcohol disorder, the comprehensiveness of these assessments will vary depending on the resources available, the specificity of the information required, the treatment setting, and the assessor's skill level. Several brief and widely available questionnaires can assess for symptoms of co-occurring disorders. These instruments include (1) the Beck Depression Inventory (Beck, Steer, & Garbin, 1988); (2) the Beck Anxiety Inventory (Beck, Epstein, Brown, & Steer, 1988); (3) the Hamilton Rating Scale for Depression (Hamilton, 1960); and (4) the Symptom Checklist-90-R (Derogatis, 1983). For brief descriptions of the clinical utility of these instruments with individuals with alcohol use disorders, readers are referred to two reviews (Carey & Correia, 1998; Sobell et al., 1994). Personality tests, especially objective tests rather than projective tests, also have clinical utility in assessing psychiatric disorder among individuals with alcohol use disorder. Prominent examples of objective personality tests include the Minnesota Multiphasic Personality Inventory–2 (Hathaway & McKinley, 1989 [revised 2001]) and the Millon Clinical Multiaxial Inventory–III (Millon, Millon, Davis, & Grossman, 2006).

High-Risk Situations and Self-Efficacy

Because relapse rates among individuals treated for alcohol problems are extremely high, the assessment of high-risk situations for drinking has long been recognized as important at assessment and during treatment (Marlatt & Gordon, 1985; Sobell & Sobell, 1993). The Situational Confidence Questionnaire (SCQ-39) assesses self-efficacy to resist drinking by asking clients to rate their self-efficacy across a variety of situations on a scale ranging from 100% confident to 0% confident. The SCQ-39 can be completed in less than 20 minutes and contains eight subscales (e.g., unpleasant emotions, pleasant emotions, testing personal control) based on the classic relapse research by Marlatt and Gordon (Marlatt & Gordon, 1985). For clinical purposes, the Brief SCQ (BSCQ), a variant of the SCQ that is easy to score and interpret, was developed and consists of eight items that represent the eight subscales (Breslin, Sobell, Sobell, & Agrawal, 2000). Although the BSCQ can be used clinically to enhance treatment planning, it only identifies generic situations and problem areas. To examine clients' individual high-risk situations or areas where they lack self-confidence, clinicians should explore in depth specific high-risk situations with clients. For example, clients can be asked to describe their two or three highest-risk situations for alcohol use in the past year, with attention to the similarities and differences across the situations. Another instrument for measuring self-efficacy to resist substance use is the Drug-Taking Confidence Questionnaire–8 (DTCQ-8; Sklar & Turner, 1999), an eight-item questionnaire similar to the BSCQ but applicable across a variety of different substance use disorders.

Neuropsychological Functioning

Numerous neurophysiological and neuropsychological studies have identified negative consequences from both acute and chronic alcohol consumption in areas of brain functioning, including attention, auditory working memory, verbal processing, abstraction/cognitive flexibility, psychomotor function, immediate memory, delayed memory, reaction time, and spatial processing (Lyvers, 2000; Oscar-Berman & Marinkovic, 2007). Moreover, it is well documented that individuals with alcohol use disorder are at elevated risk for neuropsychological problems, which can prove to be barriers to treatment success if they are not identified and addressed. Thus, a comprehensive alcohol use disorders assessment should include neuropsychological screening. Multiple screening tests are available for measuring neuropsychological functioning, but the most widely used include (a) the Digit Span, Letter Number Sequencing, and Similarities subscales from the Wechsler Adult Intelligence Scale (WAIS-III; Wechsler, 1997a); (b) the Trail Making Test (Davies, 1968); (c) the Wisconsin Card Sorting Test-64 (Kongs, Thompson, Iverson, & Heaton, 2000); and (d) the Spatial Span subscale from the Wechsler Memory Scale (WMS-III; Wechsler, 1997b). These screening tests are relatively easy and quick to administer (e.g., about five minutes) and are highly sensitive to alcohol-related brain dysfunction. For a good overview of neuropsychological assessment with individuals with alcohol use disorder, interested readers are referred to Allen, Strauss, Leany, and Donohue (2008).

BARRIERS TO CHANGE

In developing a treatment plan, it is helpful to anticipate possible barriers that clients might encounter with respect to changing their behavior. Barriers can be both motivational and practical. If an individual is not motivated to change, there is little reason to expect that change will occur. Because many alcohol abusers are coerced into treatment (e.g., courts, significant others), such individuals might not have a serious interest in changing (Cunningham, Sobell, Sobell, & Gaskin, 1994). Thus, it is important to evaluate a client's motivation for and commitment to change. According to Miller and Rollnick (1991), "motivation is a state of readiness or eagerness to change, which may fluctuate from one time or situation to another. This state is one that can be influenced" (p. 14). Thus, rather than a trait, motivation is a state that can be influenced by several variables, one of which is the therapist.

An easy way to assess readiness to change is to use a Readiness Ruler (see p. 139; SAMHSA, 1999). The Readiness Ruler asks clients to indicate their readiness to change using a 5-point scale ranging from "not ready to change" to "unsure" to "very ready to change." The ruler has face validity, is user friendly, and takes only a few seconds to complete. For a detailed description of methods for increasing motivation for change, readers are referred to two excellent resources (Miller & Rollnick, 2002; SAMHSA, 1999). Environmental factors can also present formidable obstacles to change. For example, individuals in an environment where alcohol is readily available and where there are many cues to drink might find it difficult to abstain. For some individuals, social avoidance strategies (e.g., avoiding bars, no alcohol in the house) might be the only effective alternative. Finally, clinicians should attend to individual barriers that can also affect a person's ability to enter and complete treatment (e.g., child care, transportation, inability to take time off from work, unwillingness to adopt an abstinence goal) (Schmidt & Weisner, 1995).

BIOCHEMICAL MEASURES

Both unintentional and intentional recall biases can lead to inaccuracies in the self-report measurement of alcohol use. The use of alcohol, tobacco, and other drugs can be detected in different bodily fluids (e.g., breath, blood, urine, hair, saliva) and by several biochemical detection methods. In situations where there are concerns about the validity of self-reports (e.g., drug use among criminal offenders), a convergent validity approach relying on biochemical measures is often employed. Although there has been a tendency to consider biochemical measures as "gold standards" that are superior to self-reports, it is important to note that biochemical measures can suffer from validity and implementation problems. In fact, in some settings, self-reports may be superior to certain biochemical measures (Gmel, Wicki, Rehm, & Heeb, 2008). Moreover, issues of self-report accuracy take on different meanings for clinical versus research purposes, where different levels of reporting precision are required. For example, clinicians do not routinely have to obtain information to confirm their clients' alcohol use unless the situation warrants it. However, in clinical trials, researchers typically choose to verify their clients' self-reports using biochemical or other alternative measures (e.g., collateral reports).

Urinalysis can provide qualitative (i.e., which substances are currently in the body) and quantitative (i.e., how much of a substance is currently in the body) information.

The detection of alcohol in the urine typically uses Ethyl glucuronide (EtG), a direct metabolite of ethanol alcohol. EtG is present in the urine roughly 80 hours after alcohol has been metabolized. Given its relatively high reliability and sensitivity, and low expense, EtG testing is often used in situations where alcohol consumption is prohibited, such as by the military or in recovering alcoholic patients. However, all urine tests have limitations. Urinalyses cannot specify when a drug was taken. Rather, it only provides evidence of whether consumption occurred and the amount of drug or the drug's metabolite in the system at the time of testing. Moreover, urine tests are not able to distinguish between alcohol absorbed into the body from the actual consumption of alcohol versus exposure to any of the many common commercial and household products containing alcohol. A final problem with urine testing is the urine specimen itself, which can be embarrassing to obtain, be adulterated or substituted, and present a biological hazard during shipping and disposal.

Breath and hair analysis can also provide reliable information on alcohol use. A breath analyzer will yield reasonably accurate readings of a person's blood alcohol concentration (BAC), which is measured indirectly by analyzing the amount of alcohol in one's breath. Breath alcohol testers are noninvasive, inexpensive, easy to use, portable, and provide an immediate determination of BAC. Several portable testers differing in cost and precision are commercially available. Although they are relatively robust measures of BAC, breath analyzers can produce false readings due to tobacco smoke, recent drinking, a person's breathing rate, or equipment or operator error. Hair analysis tests whether two markers of alcohol use, ethyl glucuronide (EtG) and fatty acid ethyl esters (FAEEs), are present. Only scalp hair can be used, and a sample approximately the diameter of a pencil and about 1.5 inches long is required. Hair analysis is relatively noninvasive and highly accurate, and it can provide a history of alcohol consumption for up to several years. Moreover, hair samples are nearly impossible to adulterate and are highly stable and transportable. Despite these advantages, hair analysis is several times more expensive than urine analysis, and it will not work if a person has very short hair or a shaved head.

Liver function problems are highly prevalent in alcoholics (Lucey, Mathurin, & Morgan, 2009), so physicians routinely assess hepatic dysfunction when presented with a patient with chronic drinking problems. Elevated liver enzymes, which indicate liver dysfunction, are seen among alcohol-dependent drinkers. However, most problem drinkers (i.e., those who are not severely dependent on alcohol) do not show elevations on liver function tests (Sobell, Agrawal, & Sobell, 1999). In addition, alcohol-dependent women, more than alcoholic men, are likely to demonstrate hepatic dysfunction (Wagnerberger, Schafer, Schwarz, Bode, & Parlesak, 2008). Cirrhosis, permanent and nonreversible cellular liver damage (Maher, 1997), occurs typically among only those with the heaviest drinking patterns. Unlike assessment of acute hepatic dysfunction, which can be done through a blood test, cirrhosis must be diagnosed through a liver biopsy.

ETIOLOGICAL CONSIDERATIONS

Behavioral Genetics and Molecular Genetics

Risk for alcohol use disorder involves genetic influences and environmental influences to an approximately equal extent (Enoch, Schuckit, Johnson, & Goldman, 2003;

Knopik et al., 2004; Schuckit, 2000). Close relatives of persons with alcohol problems, adopted-away children of men and women with alcohol problems, and identical twins whose parents had alcohol problems all have been found to demonstrate a much higher likelihood of experiencing alcohol use problems than the general population (Foroud, Edenberg, & Crabbe, 2010). Several endophenotypes—or subconditions that increase the risk for a disorder—have been identified in regard to alcohol problems, and these endophenotypes appear to have strong genetic influences (Puls & Gallinat, 2008; Schuckit, 2000). The absence or limited production of alcohol-metabolizing enzymes (most common among Asians), low response level to alcohol (i.e., needing a greater number of drinks to have an effect), low amplitude of the P300 wave component of event-related potentials, and low alpha activity and voltage on electroencephalograms all are associated with an increased risk of drinking problems, and all have strong genetic influences.

With regard to specific genes, the genes encoding two alcohol-metabolizing enzymes—alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH)—appear to have the strongest relation to alcohol use disorder; other gene variants associated with alcohol use disorder demonstrate much weaker relations (Foroud et al., 2010). In terms of mechanisms of action, the genetic variants associated with alcohol use disorder affect the metabolism and pharmacokinetics of alcohol, as well as the subjective response to alcohol (Heath and Martin, 1991; Ray, MacKillop, & Monti, 2010; Viken, Rose, Morzorati, Christian, & Li, 2003). Although genetic studies have documented genetic influences on the risk of alcohol problems in men, this has occurred less so with women (McGue, 1999; Prescott, 2002). In a notable exception, Hardie, Moss, and Lynch (2008) found provisional support for gender differences in heritability with regard to specific symptoms of alcohol use problems. Despite the strong association between genetic risk and the development of alcohol use disorder, it is important to remember that a wide array of environmental influences condition whether and how that risk is expressed (Johnson, van den Bree, Gupman, & Pickens, 1998).

Neuroanatomy and Neurobiology

Multiple biological and physiological systems are impacted by and appear to influence alcohol consumption. As reviewed earlier, biological factors found to be associated with the development of alcohol problems include the absence or limited production of alcohol-metabolizing enzymes, low level of response to alcohol (i.e., needing more drinks to have an effect), low amplitude of the P300 wave component of event-related potentials, and low alpha activity and voltage on electroencephalograms. These factors all substantially raise the likelihood that an individual will develop alcohol problems, but none, alone or in combination, is a sufficient or necessary determinant of alcohol abuse or dependence.

In addition, two other biological systems are currently receiving considerable research attention. The hypothalamic-pituitary-adrenal (HPA) axis is a hormone system that plays a central role in the body's response to stress. Alcohol consumption has been shown to stimulate the HPA axis system, and several studies suggest that individuals who demonstrate greater HPA activity in response to various stimuli may find alcohol consumption more reinforcing than individuals who demonstrate lower

HPA activity (Gianoulakis, 1998; Kiefer, Jahn, Schick, & Wiedemann, 2002). However, it is important to note that there are large individual differences in the response of the HPA axis to either stress or alcohol, and HPA dysfunction may play a role in only a subgroup of individuals with alcohol use problems (Sillaber & Henniger, 2004). The endogenous opioid system plays a central role in various physiological processes, including pain relief, euphoria, and the rewarding and reinforcing effect of psychoactive substances (Volkow, 2010). Alcohol consumption also stimulates the endogenous opioid system, and it appears that endogenous opioids help mediate the reinforcing effects of alcohol (Gianoulakis, 1998; Le Merrer, Becker, Befort, & Kieffer, 2009). Specifically, alcohol consumption increases dopamine in the nucleus accumbens (NAc), which may account for some of its reinforcing effects among some individuals. As with HPA, the endogenous opioid system may be most influential among a subgroup of individuals with alcohol use problems (Volkow, 2010).

Learning, Modeling, and Life Events

Learning theory, as applied to alcohol use, assumes that drinking is largely learned and that basic learning principles guide the acquisition, maintenance, and modification of drinking behavior (Carroll, 1999). Classical conditioning models posit that the development of a drinking problem occurs largely through the pairing of conditioned stimuli, such as locations or people, with the unconditioned stimulus of alcohol (Hesselbrock, Hesselbrock, & Epstein, 1999). Through repeated pairings with alcohol, the conditioned stimuli come to elicit a conditioned response, which is manifested in craving for alcohol. Tolerance to alcohol also has been explained using a classical conditioning model, where the conditioned stimuli come to elicit a conditioned compensatory response (i.e., an opposite reaction to the initial drug effects) that resembles the unconditioned compensatory response elicited by alcohol consumption (Sherman, Jorenby, & Baker, 1988; Wikler, 1973). Operant conditioning models assume that alcohol consumption is governed by its reinforcing effects, including physiological and phenomenological changes in response to drinking, the social consequences of drinking, and/or the avoidance or cessation of withdrawal symptoms (Hesselbrock et al., 1999). In summary, learning models may explain how drinking problems may develop and provide guidance in the design of interventions designed to modify drinking.

An especially influential variable in alcohol use and abuse that appears to be governed by basic learning principles is alcohol expectancies. Alcohol expectancies are the effects (positive and negative) attributed to alcohol that an individual anticipates experiencing when drinking (Goldman, Del Boca, & Darkes, 1999). Expectancies appear to develop early in life, are consistent across gender, and are learned according to social learning principles, including classical conditioning, operant conditioning, and modeling (Hesselbrock et al., 1999). In several different studies, alcohol expectancies have been shown to be highly related to adult and adolescent drinking practices, including drinking problems and relapse to drinking following a period of abstinence (Marlatt & Witkiewitz, 2005; Witkiewitz & Marlatt, 2007).

Research on the modeling of alcohol consumption emerged from Bandura's (1969) social learning theory, which posits that modeling influences the acquisition and performance of a variety of social behaviors. Caudill and Marlatt (1975) were among

the first to experimentally study the influence of social modeling on drinking behavior, and they found that participants exposed to a heavy drinking model (a research confederate) consumed significantly more wine than participants exposed to a light drinking or no model. Collins and Marlatt (1981) reviewed the research in 1981 and concluded that modeling was a powerful influence on drinking that occurred regardless of study setting or moderating variables (e.g., gender, age). More recently, Quigley and Collins (1999) performed a meta-analysis on published studies concerning the modeling of alcohol consumption and found "a definitive effect" of modeling on drinking behavior. Large effect sizes for both amount of alcohol consumed and BAC were documented. Modeling effects appear to be particularly influential among underage and young adult drinkers (Ennett et al., 2008).

For centuries, stress from life events has been thought to be related to alcohol consumption, and drinking has been seen as relieving stress (Sayette, 1999). The relationship between drinking and stress can be traced to the sociological literature of the 1940s and the emergence of the tension-reduction hypothesis in the 1950s (Pohorecky, 1991). The tension-reduction hypothesis proposes that (a) alcohol consumption will reduce stress under most circumstances, and (b) people will be motivated to drink in times of stress. This hypothesis forms the basis of current research about the relationship between drinking and stress (Sayette, 1999). Although studies indicate that drinking can reduce stress related to life events in certain people and under certain circumstances, the relationship between drinking and life events is far more complex than originally thought. Individual differences, including a family history of alcohol problems, certain personality traits (e.g., impulsivity), extent of self-consciousness, level of cognitive functioning, gender, and situational factors including distraction and the timing of drinking and stress, have all been shown to be important moderators of the degree to which alcohol will reduce the subjective, behavioral, neurochemical, and immunological consequences of stress (Fox, Bergquist, Gu, & Sinha, 2010; Hussong, Hicks, Levy, & Curran, 2001; Sayette, 1999).

Cognitive Influences

An extensive literature exists regarding the role of cognitive influences on alcohol use. Among the earliest cognitive models of alcohol use is Hull's (1981) Self-Awareness Model. This model proposes that alcohol interferes with the process of encoding information, which subsequently decreases self-awareness by preventing the encoding of failures or poor evaluative feedback. Furthermore, the Self-Awareness Model postulates that people drink to reduce self-evaluative forms of stress. Although influential in stimulating research on cognitive influences on alcohol use problems, empirical evidence in support of the Self-Awareness Model has been inconsistent (Bacon & Ham, 2010), and other cognitive models subsequently have been proposed. The Attentional Allocation Model and Appraisal Disruption Model are especially notable.

Steele and Josephs' (1988, 1990; Josephs & Steele, 1990) Attentional Allocation Model proposes that alcohol consumption reduces an individual's capacity for controlled and effortful information processing and for paying attention. Alcohol consumption results in "alcohol myopia," where attention is focused only on cues that are immediately salient and require little effortful processing. Depending on how

attention is focused during intoxication (e.g., on a distraction or on current stressors), attention allocation can account for both increases and decreases in perceived stress and subjective well-being from drinking. Sayette's (1993) Appraisal-Disruption Model includes aspects of both the Self-Awareness Model and the Attention-Allocation Model, but it uniquely proposes that alcohol interferes with cognitive processing at the level of appraisal, which occurs early in information processing and involves the determination of the personal valence and relevance of stimuli and cues. The Appraisal-Disruption Model focuses on alcohol's effects on information organization, as opposed to self-awareness or attentional allocation, and includes a temporal dimension (i.e., before or during intoxication) in predicting how cue appraisal will influence drinking and its subjective consequences.

Sex and Racial-Ethnic Considerations

Whenever and wherever women's and men's alcohol use has been measured, results show that women drink less than men, and women's drinking leads to fewer social problems than men's drinking (NIAAA, 2005; Wilsnack, Vogeltanz, Wilsnack, & Harris, 2000). However, few studies go beyond demonstrating that men use and have problems with alcohol more than women do, and currently both biological and social-structural theoretical explanations exist for these gender differences (Wilsnack et al., 2000). The biological explanations emphasize gender differences in the metabolism of alcohol, and the social-structural explanations emphasize gender differences in social roles, and how these differences may influence drinking behavior. With regard to biological explanations, several animal studies have documented gender differences in alcohol metabolism, and it appears that hormonal differences between the sexes may modulate these differences (Smith & Lin, 1996). Moreover, women are more susceptible to alcoholic liver injury than are men, and this appears to be the result of less metabolism of alcohol in the stomach, and thus greater exposure to high alcohol concentrations (Frezza et al., 1990; Moack & Anton, 1999; Morgan, 1994; Schenker, 1997). Whereas research has suggested that women's reproductive functioning influences alcohol metabolism, evidence is mixed regarding how menstrual cycle phase may affect alcohol consumption, metabolism, and self-estimates of blood alcohol levels (Jensvold, 1996). Although one study has suggested that the use of oral contraceptives results in decreased alcohol metabolism, and thus increased alcohol effects (Jones & Jones, 1976), another study found no effect of oral contraceptives on alcohol metabolism (Hobbes, Boutagy, & Shenfield, 1985).

With regard to social-structural explanations, some investigators have examined how women's social roles vis-à-vis alcohol may explain lower rates of alcohol use and abuse among women than men. Cross-culturally, women's drinking has been more socially restricted than their male counterparts, primarily because it may negatively affect women's social behavior and responsibilities (Wilsnack et al., 2000). Consistent with this perspective, there is evidence that social influences play a greater role in women's than men's drinking. For example, partners' heavy drinking has a greater influence on female problem drinking than on male problem drinking (Gomberg, 1994), and there is more marital disruption (i.e., never married, divorced or separated, widowed) among females (Gomberg, 1995). Moreover, a recent study indicates that the types of problems experienced by women with alcohol use disorder differ from

those experienced by men with alcohol use disorder. Nichol, Krueger, and Iacono (2007) found that one-third of the symptoms typically used to diagnose alcohol problems concerned problems experienced almost exclusively by males (e.g., fighting while drinking). In addition, depression appears to be particularly associated with women's drinking and drinking problems (Conner, Pinquart, & Gamble, 2009; Nichol et al., 2007). This speaks to the need for more sensitive indices for detecting drinking problems among women, with an emphasis on depressed affect. In sum, it appears that both biological and social-structural explanations may be needed to account for gender differences in alcohol use and abuse.

Regarding race and ethnicity, epidemiological studies show that alcohol use, morbidity, and mortality vary by race/ethnicity in seemingly paradoxical ways. For example, African Americans and some Hispanic/Latino groups have lower overall rates of alcohol involvement than do non-Latino Whites, yet these groups demonstrate higher rates of alcohol-related morbidity and mortality than do non-Latino Whites (Caetano, 2003; Gilliland, Becker, Samet, & Key, 1995; Lee, Markides, & Ray, 1997). This paradox may result from ethnic/racial variations in the processes by which alcohol use can lead to alcohol problems. For example, the accelerated progression from use to problem use seen among these minority populations could result from socioeconomic polarization, criminal justice problems, or the lack of appropriate treatment options. Compared with other ethnic groups, (a) Native Americans and Hispanics report higher rates of high-risk drinking; (b) Native Americans and Whites have a greater risk for alcohol use disorders; (c) Native Americans, Hispanics, and Blacks experience more severe drinking-related consequences; and (d) Hispanic problem drinkers are less likely to enter and stay in treatment (Chartier & Caetano, 2010). Moreover, among alcohol-dependent drinkers, Blacks and Hispanics are more likely to demonstrate recurrent or persistent alcohol dependence. Additional factors that may affect how race and ethnicity are associated with the progression to alcohol problems, as well as with response to alcohol abuse treatment, include perceived discrimination and cultural mistrust for African Americans, and acculturation stress, nativity, and immigration history for Hispanics/Latinos.

COURSE AND PROGNOSIS

Based largely on Jellinek's work on the progression of alcoholism (Jellinek, 1952), mid-20th-century thinking about the course of alcohol problems was that such problems develop in early adulthood (i.e., 20 to 30 years of age) and increase in severity over the course of several years. As noted earlier in this chapter, the notion of progressivity in alcohol problems has not been supported by research, although some alcohol problems do worsen over time. Research also shows that alcohol problems can occur at any age (Atkinson, 1994; Schonfeld & Dupree, 1991; Schuckit & Smith, 2011; Wilsnack, Klassen, Schur, & Wilsnack, 1991). The temporal pattern can be variable, with problems sometimes remitting, worsening, or improving (Cahalan & Room, 1974; Dawson, 1996; DeLucchi & Kaskutas, 2010; Hasin et al., 1990; Mandell, 1983). If an individual is experiencing alcohol problems at one point, it is not possible to predict that, in the absence of treatment, the problem will worsen. It has been found, however, that men whose alcohol problems are severe are likely to continue to worsen over time if they continue to drink (Fillmore & Midanik, 1984). More recent research indicates

that gender differences in the course of alcohol use and alcohol use problems are decreasing among younger cohorts, whereas gender differences in time from first use to dependence are increasing, with an accelerated time to dependence among men (Keyes, Martins, Blanco, & Hasin, 2010).

Alcohol problems have been characterized as a recurrent disorder (Polich, Armor, & Braiker, 1981). This characteristic has given the disorder a reputation as difficult to treat and seldom cured. Recent research, however, has found that the probability of relapse in persons who have been in remission for several years is low (Finney & Moos, 2001; Schuckit & Smith, 2011; Sobell, Sobell, & Kozlowksi, 1995). Clinically, the high likelihood of recurrence has led to relapse prevention procedures (Marlatt & Gordon, 1985). Such procedures include advising clients that setbacks may occur during recovery from the disorder, and that they should use these setbacks as learning experiences to prevent future relapses, rather than as evidence that recovery is impossible. Moreover, a recent 16-year-long study of individuals treated for alcohol problems found predictors of long-term success to include first-year posttreatment engagement in AA, reduced depressive symptoms, improved stress coping, and enhanced social support for nondrinking (McKellar, Ilgen, Moos, & Moos, 2008). Finally, the presence of co-occurring psychiatric disorder(s) is associated with a more guarded prognosis for recovery among individuals treated for alcohol use disorders (Baigent, 2005; Le Fauve et al., 2004; Modesto-Lowe & Kranzler, 1999).

CASE STUDY

The following case study provides an example of a typical client presenting for outpatient treatment of alcohol use problems.

Case Identification

The patient is a 27-year-old White, single male who voluntarily entered treatment at the Guided Self-Change (GSC) Clinic at the Addiction Research Foundation (Toronto, Canada). Guided Self-Change treatment, a motivationally based cognitive-behavioral intervention, emphasizes helping clients to help themselves (Sobell & Sobell, 1993). The intervention includes an assessment, four semistructured sessions, and an aftercare component. In addition, clients are given an opportunity to request additional sessions. The GSC treatment intervention has been evaluated in several clinical trials (Sobell & Sobell, 1998).

Presenting Complaints

The patient was in his last year of graduate school and was planning to pursue a postdoctoral fellowship in the coming year. He reported seeking treatment because of "hitting a personal rock bottom" and an "ultimatum from my girlfriend." The client reported that 2 years prior to treatment, the frequency and quantity of his drinking had increased and that he had tried to cut down and stop without success. He also reported that his university friends and colleagues drank heavily after seminars, and that he perceived there was a "stigma" attached to people who left after a few drinks.

He noted that he felt pressured to drink when others around him drank. At treatment entry, he reported he was "extremely ready" to take action to change his drinking, and at the assessment he stated, "I've started working on my problem, but I need some help." When asked why he decided to seek treatment, he stated:

> A series of events which started with increased drinking, behavioral change, fights when I was intoxicated, or "drunk" for a better word, breakups with friends, stupid arguments with friends, arguments with girlfriends—Just a lot of bad times and a lot of problems. I usually go for maybe two or three weeks and say "I'm positively not going to have anything to drink," but when I would say "Okay, well I can handle this now," it seemed to get worse, so I thought it's time to talk to somebody about it.

HISTORY

Although he reported drinking heavily for 8 years, he felt that his drinking had only been a problem for the past 4 years. His score on the Alcohol Dependence Scale (ADS; Skinner & Allen, 1982) was 11 and on the Drug Abuse Screening Test (DAST-20; Skinner, 1982) was 1. An ADS score of 11 is in the first quartile for ADS norms and is reflective of someone who has a mild alcohol problem. A DAST-20 score of 1 suggests no current drug problem. The patient also reported no current use of prescription medications or other psychoactive substances, including nicotine. He reported no current health problems or past treatment for mental health or substance use problems. He also reported never having attended self-help group meetings (e.g., AA) and had no prior alcohol-related hospitalizations or arrests. He reported no morning drinking in the past year, and in terms of family history, reported that his father had had a problem with alcohol. He reported experiencing several alcohol-related consequences in the 6 months prior to the assessment (e.g., fights in bars, personal problems, verbally abusive, spending too much money on alcohol). He reported that his highest-risk situations for problem drinking were when he was home alone, bored and stressed, and when with friends after work at seminars. He also reported that on about half the days when he drank alcohol, it was when he was alone. Although this was his first treatment experience, he reported several prior attempts to quit or reduce his alcohol use.

ASSESSMENT

At the assessment, his subjective evaluation of the severity of his alcohol problem was "major," and he rated the overall quality of his life as "very unsatisfactory." Self-report of his drinking in the past year using the Timeline Followback assessment (LaBrie, Pedersen, & Earleywine, 2005; Sobell & Sobell, 1992) was (1) abstinence: 59% of the days; (2) drinks per drinking day: 4.5 standard drinks (SDs; 1 SD = 13.6 g of absolute ethanol); (3) average weekly consumption: 13 SDs; (4) highest single drinking day in the past year: 14 SDs; (5) low consumption days (1–3 SDs): 42% of all days; (6) heavy consumption: 22% of all days (20% = 4–9 SDs, 2% were 10 SDs). When shown the personalized feedback based on his self-reports of drinking (Sobell & Sobell, 1996; Sobell & Sobell, 1998; SAMHSA, 1999), he said: "I'm a little alarmed. More than a little

alarmed, but I'm alarmed that I'm at the high end, but I know that's why I'm here. The other part that alarms me is that most of the people I know, I would put them in that." Based on the assessment interview, this patient met the criteria for a *DSM-IV* diagnosis of alcohol dependence and would meet the criteria for a *DSM-5* diagnosis of alcohol use disorder. On a continuum of alcohol use problems, the severity of his problem would be evaluated as mild to moderate.

SUMMARY

Conceptualizations of alcohol problems have improved markedly over the past three decades, affecting research and practice in regard to alcohol use disorders and their treatment. In particular, it is now recognized that severely dependent alcoholics represent only a small proportion of individuals suffering with alcohol problems. A one-size-fits-all approach is no longer appropriate for all individuals with alcohol problems, and residential treatment has fallen out of favor. The concept that alcohol problems can be scaled along a continuum of severity has major implications for assessment and treatment. For example, less severely dependent alcohol abusers can benefit from brief treatment, preceded by a brief assessment. The idea of a continuum of severity suggests that treatment for alcohol problems should be provided using a stepped-care model where the first treatment is the least intensive, costly, and invasive, has demonstrated effectiveness, and is appealing and engaging to consumers. If treatment is not successful, then it can be stepped up to include longer, more intensive, or different components.

Assessment of alcohol problems is critical to good treatment planning and is a process that carries on throughout treatment. Besides using sound psychometric assessment instruments, the instruments should be clinically useful. Several important issues also need to be addressed at assessment. Paramount among these is the assessment of co-occurring psychiatric disorders and other drug and nicotine use. Although many people with alcohol problems voluntarily seek treatment, many are coerced to seek treatment (e.g., by the courts, significant others, employers). In this regard, they often exhibit resistance and a lack of commitment to change. Motivational enhancement techniques and a motivational interviewing style can be used to decrease patients' resistance and increase their commitment to change. Lastly, although alcohol problems can be treated successfully, there is still a high rate of relapse that must be addressed in treatment, but recurrence of problems should not be taken as an indication that the disorder is worsening, because there is now abundant data showing that alcohol problems are not necessarily progressive.

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CHAPTER 18

Psychoactive Substance Use Disorders: Drugs

STACEY B. DAUGHTERS and MATTHEW COHEN

DESCRIPTION OF THE DISORDER

Illicit drug use is a prevalent and pervasive issue in the United States and, as a result, substance use disorders (SUDs) incur major costs to individuals, families, and society at large. In 2008 approximately 8.9% (22.2 million) of Americans age 12 or older were classified with substance dependence or abuse in the past year, and these estimates have remained constant over the past 7 years (Substance Abuse and Mental Health Services Administration [SAMHSA], 2009a). The financial burden on society is estimated to be $484 billion annually in substance use–related treatment and prevention, health care expenditures, lost wages, reduced job production, accidents, and crime. In addition to the substantial economic cost of substance use, SUDs are associated with engagement in multiple health-compromising and risk-taking behaviors (e.g., condom nonuse, multiple partners, impulsive spending, driving while intoxicated) that contribute to the significant public health costs associated with SUDs (Office of National Drug Control Policy [ONDCP], 2004).

CLINICAL PICTURE

SUDs can result from abuse of a single drug or multiple substances. Commonly, drugs of abuse are grouped based on categories that vary in their physiological and behavioral effects. In this section we discuss the different drug categories, including street and slang names, physiological and psychological effects of each category, and the withdrawal symptoms that occur as tolerance and dependence develop. Interested readers are referred to Julien (2004) for an extensive review.

Cannabinoids, such as marijuana and hashish (street names include dope, pot, weed, grass, hash), produce mild euphoria, sedation, enhanced sensory perception, increased appetite and pulse, psychomotor impairment, and confusion. Tolerance can occur with habitual use, and discontinuation of use can result in uncomfortable withdrawal effects including anxiety, depression, irritability, and insomnia. Alternatively, hallucinogens, which include LSD (acid, blotter), mescaline (buttons, peyote,

mesc), and psilocybin (magic mushrooms, shrooms), create an altered state of consciousness, detachment from self and environment, and dissociative symptoms. Hallucinogens are not physically addictive; however, LSD and mescaline produce negative physiological reactions such as increased body temperature, blood pressure, and heart rate. Psychologically, hallucinogen use can result in persistent mental disorders characterized by panic attacks and psychosis.

Both cannabinoids and hallucinogens are illegal street drugs, but central nervous system (CNS) depressants, including alcohol, benzodiazepines (e.g., alprazolam [Xanax], diazepam [Valium], lorazepam [Ativan], clonazepam [Klonopin]; benzos, xannies), and barbiturates (Seconal, Amytal, Phenobarbital; reds, yellows, yellow jackets, barbs) are legal substances that can be obtained with a doctor's prescription. With low or moderate doses, they produce euphoria and disinhibition as well as decreased respiration, pulse, and blood pressure. At higher doses, confusion, impaired judgment, coordination, and memory loss occur. CNS depressants are particularly dangerous when combined because this increases the risk of respiratory depression and arrest. With long-term use, tolerance occurs and discontinuation of use can cause symptoms ranging from anxiety, insomnia, nausea, and muscle tension to more severe symptoms such as seizures, hallucinations, and psychosis.

Opioids are often prescribed for pain relief (e.g., codeine, fentanyl, oxycodone), but these drugs are also commonly abused. Other drugs in this category include opium (big O, tar) and heroin (dope, H, junk, smack). The effects of intoxication include euphoria, sedation, drowsiness, confusion, nausea, constipation, and respiratory depression. High doses of opioids can lead to coma and death. With prolonged use, tolerance occurs and, in the absence of the drug, users experience craving, sweating, fever, diarrhea, vomiting, and pain.

Unlike CNS depressants and opiates, stimulants increase respiration, heart rate, and blood pressure, and decrease appetite. Stimulant intoxication produces euphoria, mental alertness, and increased energy. Impulsive behavior, aggressiveness, anxiety, and irritability are also common features experienced by users. Additionally, prolonged use or high doses of stimulants can result in stimulant-induced psychosis. Due to the stress placed on the cardiovascular system, stimulant use can cause cardiac arrest, stroke, and death. Stimulants include cocaine (crack, coke, blow, yayo), methamphetamine (meth, speed, crystal, crank), MDMA (ecstasy, E, X, Adam), amphetamines (Adderall, Dexedrine; speed), and methylphenidate (Ritalin, vitamin R). Nicotine, found in cigarettes, cigars, and smokeless tobacco (snuff, dip, spit) is also a stimulant. Tolerance occurs quickly and can often lead to dependence. Withdrawal symptoms include anxiety, anhedonia, irritability, insomnia, and depression.

Dissociative anesthetics, such as ketamine (Special K, vitamin K) and PCP (angel dust, hog, love boat, sherms), create a dream-like state, euphoria, numbness, increased heart rate and blood pressure, and impaired memory and motor function. At high doses, ketamine can cause delirium, respiratory depression, and arrest. PCP use can result in panic, aggression, depression, and violence. Users of dissociative anesthetics quickly experience increasing tolerance, and a permanent tolerance may develop after several months of use. Although tolerance occurs, these drugs do not appear to have withdrawal symptoms or dependence.

Inhalants include a range of solvents (glues, paint thinners, gasoline), gases (propane, butane, aerosol propellants, nitrous oxide; laughing gas, whippets), nitrates

(isobutyl, isoamyl; poppers, snappers), and aerosols (hair spray, spray paint). Inhalants are "huffed" through the nose and mouth and enter the lungs and subsequently the bloodstream rather quickly. The effects of intoxication include loss of motor skills and inhibition, slurred speech, headache, nausea, wheezing, and loss of consciousness. Extended use can lead to muscle weakness, memory impairment, depression, damage to the nervous and cardiovascular systems, and sudden death. There is little known about tolerance, withdrawal, and dependence in relation to inhalants.

In summary, once an SUD is present, the withdrawal experience from different substances varies by the class of drug. In general, common psychological features of withdrawal involve symptoms of depression and anxiety. Although the physical symptoms of withdrawal can be difficult to tolerate, they are often short lived.

DIAGNOSTIC CONSIDERATIONS

The *Diagnostic and Statistical Manual* (*DSM-5*; American Psychiatric Association [APA], 2013) provides a comprehensive classification system for the assessment and subsequent diagnosis of a *substance use disorder* across 10 drug classes including alcohol, cannabis, phencyclidine, other hallucinogens, inhalants, opioids, sedatives, stimulants, tobacco, and other/unknown. The *DSM-5* diagnostic criteria for a substance use disorder require evidence of continued use in spite of significant substance-related problems. A key characteristic of a substance use disorder is a change in the user's neurological circuitry, a side effect that persists even in times of post-use sobriety. This altered circuitry is believed to manifest itself in the user's behavior and can therefore be linked to relapse.

The *DSM-5* diagnostic criteria for substance use disorders specify a maladaptive pattern of behaviors related to substance use. These behaviors fall into four categories: *impaired control, social impairment, risky use,* and *pharmacological criteria.* Impaired control is often characterized by unsuccessful efforts to follow through with intended plans to cut back on use, taking more than planned, or use for a greater duration than initially planned. Impaired control can involve craving, a perceived need to engage in substance use, often arising in the context of prior use (e.g., the presence of people with whom one had used; being in a location where one had previously used). Craving is operationalized as the extent to which the desire to use consumes the patient's thoughts. *Social impairment* pertains to an inability to carry out the needs of daily life in all facets of one's environment, whether it involves failing to fulfill obligations or opting to use rather than engaging in social activities. Further, in spite of the negative impact that using may have, social impairment is characterized by persistent substance use in spite of the negative social impact. *Risky use* involves the continued use of a substance that is known to present a danger to the user. This risk might entail using in a dangerous situation or using with a known vulnerability to a physical or psychological issue that would likely be made worse by further use. *Pharmacological criteria* focuses on tolerance and withdrawal. Tolerance is a state that develops wherein the user needs progressively larger doses of the drug in order to feel the desired effect. Withdrawal is a physical response to specific substances that can occur after extended, consistent use. The diagnostic criteria for substance use disorders specify that at any given time the presence of two to three symptoms suggest mild substance abuse disorder with moderate (four to five

symptoms) and severe disorders (six or more symptoms) requiring greater symptomology.

Another system, the *International Classification of Diseases*, 10th revision (*ICD-10*; World Health Organization [WHO], 1994), is considered the international standard diagnostic classification system for all general epidemiological and many health management purposes, including the analysis of the general health situation of population groups and monitoring of the incidence and prevalence of diseases in relation to social, biological, and interpersonal variables. Although there is overlap in the way that the *DSM* and *ICD* view substance use disorders, the two systems have had different paradigms for maladaptive substance use that do not align well. Most notably, the *DSM-5* characterizes substance use by negative social consequences of recurrent or continued use, whereas the *ICD-10* includes a category for harmful use (a nonresidual category), which requires demonstrable physical or psychological harm. The emphasis on physical or psychological harm (rather than legal and social) in the *ICD-10* stems from a need for developing criteria that can be applied uniformly across different countries and cultures.

Substance use disorders co-occur with many clinical disorders, ranging from depression and anxiety disorders to personality disorders. National epidemiological data suggest that among individuals with any SUD, the prevalence for any mood or anxiety disorder is 40.9% and 29.9% respectively (Conway, Compton, Stinson, & Grant, 2006). Mood and anxiety disorders are the most common comorbidities, followed by antisocial personality disorder (Jane-Llopis & Matysina, 2006) and schizophrenia-spectrum disorders (Kushner, Abrams, & Borchardt, 2000). Among personality disorders, borderline and antisocial personality disorders have the highest rates of co-occurrence with SUDs, with estimates ranging from 5% to 32% and 14% to 69%, respectively (e.g., Goldstein et al., 2007; Trull, Sher, Minks-Brown, Durbin, & Burr, 2000). In fact, estimates from the Epidemiologic Catchment Area (ECA) Survey suggest that SUDs are more strongly associated with antisocial personality disorder than with any other mood, anxiety, or thought disorder (Regier et al., 1993). Additionally, prevalence of disorders differs by substance. For example, among individuals with lifetime opioid abuse or dependence, nearly 50% met the criteria for a personality disorder (Grella, Karno, Warda, Niv, & Moore, 2009). These statistics are particularly alarming given that individuals with co-occurring disorders generally have worse treatment outcomes (e.g., noncompliance and relapse), higher rates of suicidal ideation, distorted perception and cognition, social exclusion, aggression, and homelessness (Horsfall, Cleary, Hunt, & Walter, 2009). The causal direction of co-occurring conditions is mixed, with some evidence of mental disorders predicting the onset of SUDs, while other studies have found that SUDs predict later mental illness (Kessler, 2004; National Institute on Drug Abuse [NIDA], 2009).

EPIDEMIOLOGY

Approximately 20.1 million (8%) Americans age 12 or older report illicit drug use in the past month, of which 57.3% report using only marijuana and 42.7% report illicit drug use other than marijuana (SAMHSA, 2009b). Specific populations are more vulnerable to initiation and continued illicit drug use. In particular, youth and young adults are a special population of interest, because early use increases the likelihood of

future substance use problems. Data from the Monitoring the Future Study indicates that although use of several drugs (including inhalants, ecstasy, and amphetamines) has declined over the past decade, within the past 2 years marijuana use has increased. Approximately 12% of 8th graders, 27% of 10th graders, and 33% of 12th graders reported marijuana use in the past year. Respectively, about 15%, 29%, and 37% reported using any illicit drug in the past year (Johnston, O'Malley, Bachman, & Schulenberg, 2010).

In 2007, there were more than 1.8 million admissions to treatment, with the majority of these admissions being for alcohol only or alcohol and a secondary substance (SAMHSA, 2009b). Among the different treatment settings available, most admissions were in ambulatory care (62.3%), which is made up of outpatient (49.4%), intensive outpatient (10.6%), and detoxification (2.2%). Additionally, 18% of admissions entered residential treatment, with the majority in short-term treatment (less than 31 days), and 19.7% of admissions were for short detoxification (24-hour service) (SAMHSA, 2009b).

PSYCHOLOGICAL AND BIOLOGICAL ASSESSMENT

Several variables need to be considered when determining the best method of assessment for patients with substance use problems. It is important to determine if the goal of the assessment is to screen for potential substance use problems, to determine if an individual meets diagnostic criteria for an SUD, to develop treatment goals and a treatment plan, or to assess treatment outcome. Outlined in Table 18.1 are commonly used psychological measures for screening, diagnosis, treatment planning, and posttreatment outcome measurement.

Given the high rate of comorbidity between SUD and other psychological disorders, particularly mood, anxiety, or thought disorders, patients often present to treatment for problems other than drug dependence. As such, screening measures are useful for identifying SUDs in other settings. Several diagnostic instruments are available for use in both research and clinical settings, with advantages and disadvantages inherent in each instrument with regard to administration, cost, and interviewer qualification and training requirements.

Once a substance use problem or diagnosis is established, it is important to assess how the patient's level of substance use has affected other life areas (e.g., social and occupational functioning) in order to develop appropriate treatment goals and a treatment plan. For example, by assessing how much time the patient spends obtaining and using the substance, in addition to time spent recovering, the clinician will likely gain a better sense of the extent of impairment and as such, which intervention might be most efficacious. Additional assessment techniques are utilized prior to and during treatment to target processes such as treatment planning, utilization of services, and goal attainment. It has been suggested that assessing one's readiness for change prior to developing a treatment plan will improve treatment outcomes (DiClemente & Prochaska, 1998). Accordingly, the transtheoretical model (TTM) argues that the individual moves through five stages when changing behaviors: precontemplation, contemplation, preparation, action, and maintenance.

Functional analysis often is used in substance use treatment to help patients effectively problem-solve ways to reduce the probability of future drug use. Within

Table 18.1
Instruments for the Screening and Diagnosis of Substance Use Disorders

Instrument	Summary	Method of Administration	Population
Screening			
Alcohol Use Disorders Identification Test (AUDIT; Saunders, Aasland, & Babor, 1993)	Developed by WHO, the AUDIT screens for increased risk for hazardous drinking and can identify problem drinking and dependence.	Interview, self-administered and computerized versions.	Adults; Validated cross-culturally; translated into many languages
Drug Use Disorders Identification Test (DUDIT; Stuart, Moore, & Kahler, 2003)	An 11-item measure to screen for drug-related problems across the following drug classes: cannabis, cocaine, hallucinogens, stimulants, sedatives, and opiates.	Self-report	Adults
CAGE (Cooney, Zweben, & Fleming, 1995)	Consists of four questions used to screen for a substance use problem. Each "have you ever?" question can be answered either "YES" or "NO," and each positive response gets 1 point. A score of 1 out of 4 indicates "possible" and 2 detects most cases of substance misuse. However, may not be sensitive enough to capture binge drinkers.	Interview	Adults; Adolescents
Drug Abuse Screening Test (DAST; Skinner, 1982)	Focuses on lifetime severity of drug abuse and its consequences and provides an index of drug use severity. Covers a variety of consequences related to drug use without specifying drug type, alleviating the necessity of using different instruments specific to each drug.	Interview or self-administered	Adults
MCMI-III (Millon & Meagher, 2004)	Short 14-item drug dependence scale. High scores on this scale suggest a recurrent or recent history of drug abuse, a tendency to have poor impulse control, and an inability to manage the consequences of drug use and impulsive behavior.	Self-report	Adults
Addiction Potential Scale (APS) of the MMPI-2 (Weed, Butcher, & McKenna, 1992)	This measure does not directly assess substance use behavior, but was designed to identify personality characteristics and lifestyle patterns that are associated with substance abuse.	Self-report	Adults

Simple Screening Instrument for Substance Abuse (SSI-SA; SAMHSA, 2005)	The SSI-SA screens for five domains of substance use including substance consumption, preoccupation and loss of control, adverse consequences, problem recognition, and tolerance and withdrawal.	Interview or self-administered	Adults; Co-occurring disorders
Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST; Ali et al., 2002)	Developed by WHO, the ASSIST uses eight questions to screen for tobacco, alcohol, and illicit drug use. Additional items assess problems related to substance use, the risk of current or future harm, level of dependence, and method of use (e.g., needle injection).	Interview or self-administered	Adults
Diagnostic Status			
Structured Clinical Interview for DSM-5 (SCID-5; revision pending)	The SCID is a precise method for identifying substance dependence across 10 drug classes and is the most frequently used instrument in clinical trials.	Interview; Clinician administered	Adults; Adolescents
Substance Dependence Severity Scale (SDSS; Miele et al., 2000)	Assesses both the frequency and severity of symptoms. For each symptom, the SDSS measures total number of days a symptom occurred, usual severity of the symptom, and worst severity of the symptom over a 30-day time frame.	Interview; Clinician-administered	Adults; Adolescents
Composite International Diagnostic Interview–Second Edition (CIDI-2; Kessler & Üstün, 2004)	Structured interview that provides lifetime diagnoses for past and current substance use disorders according to both the *DSM-IV* and *ICD-10*. An SUD diagnosis from the CIDI has demonstrated good reliability and validity and can be administered by a lay interviewer in approximately 20 to 30 minutes. There is not yet an updated version for *DSM-5*.	Interview	Adults; Adolescents
Treatment Planning and Outcome			
Addiction Severity Index (ASI; McLellan et al., 1992)	The most comprehensive and widely used measure. The ASI assesses drug and alcohol use in the context of seven domains: medical status, employment	Interview or self-report	Adults

(*continued*)

Table 18.1
continued

Instrument	Summary	Method of Administration	Population
	status, family history, legal status, psychiatric status, and family and social relationships. It identifies problem areas in need of targeted intervention and is often used in clinical settings for treatment planning and outcome evaluation.		
Drug Use Screening Inventory (DUSI; Tarter, 1991)	Measures the severity of drug and alcohol problem in 10 psychosocial and psychiatric domains: behavior patterns, drug consequences, health status, psychiatric disorder, social competency, family system, school performance, work adjustments, recreation, and peer relationships. A "lie scale" is built in to ensure truthfulness and increase reliability by identifying inconsistencies.	Interview or self-report	Adults; Adolescents
Inventory of Drug Use Consequences (InDUC; Tonigan & Miller, 2002)	An inventory of drug-related consequences. The InDUC is distinct from screening instruments in that it measures adverse consequences of substance use including items referring to pathological use practices (e.g., rapid use), items reflecting dependence symptoms (e.g., craving), and items concerning help-seeking (e.g., Narcotics Anonymous). Includes five scales including impulse control, social responsibility, and physical, interpersonal, and intrapersonal domains.	Self-report	Adults
Timeline Followback (TLFB; Fals-Stewart, O'Farrell, & Freitas, 2000)	Assesses recent substance use by asking the client to retrospectively report use in a defined period prior to the interview date. In addition to capturing use, the TLFB can also identify frequency of use.	Interview or self-report	Adults; Adolescents
Form 90D (Westerberg, Tonigan, & Miller, 1998)	Using a calendar, this semi-structured interview captures substance use for the past 90 days.	Clinician-administered	Adults; Adolescents

Motivation and Treatment Readiness			
University of Rhode Island Change Assessment (URICA; McConnaughy, Prochaska, & Velicer, 1983)	Measures the Stages of Change (Precontemplation, Contemplation, Action, and Maintenance) using a 5-point Likert scale. Assesses readiness to change when clients enter treatment.	Self-report	Adults; Co-occurring disorders
Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES; Miller & Tonigan, 1996)	Scale used to assess motivation for change, in relation to alcohol and drug use, using three factorially derived scores: Recognition, Ambivalence, and Taking Steps.	Self-report	Adults
Readiness to Change Questionnaire (RTCQ; Rollnick, Heather, Gold, & Hall, 1992)	Uses Stages of Change Model to assign substance users to three stages: precontemplation, contemplation, and action.	Interview	Adults; Adolescents

this model, an analysis of the antecedents and consequences of drug use is used to develop alternative cognitive and behavioral skills to reduce the risk of future drug use. Working together, the therapist and patient identify five high-risk situations and the (1) trigger for that situation, (2) thoughts during that situation, (3) feelings experienced in response to the trigger and thoughts, (4) drug use behavior, and (5) positive and negative consequences of drug use. After analyzing this behavior chain, the therapist and patient then develop strategies for altering thoughts and behaviors when faced with those same situations. Those interested in the use of functional analysis in treatment are directed to Monti, Kadden, Rohsenhow, Cooney, and Abrams (2002) or the National Institute on Drug Abuse online publication *A Community Reinforcement Approach: Treating Cocaine Addiction.*

Outcome assessments should include a wide range of dimensions beyond substance use behavior, including changes in social, occupational, and psychological functioning. As such, it is ideal to readminister comprehensive measures such as the *Addiction Severity Index*, *Drug Use Screening Inventory*, and *Inventory of Drug Use Consequences* (see Table 18.1). In addition, self-report and biological indicators can be used to determine return to drug use, drug use behavior, and psychiatric symptoms.

The following is a brief overview of recent trends in the biological assessment of substance use (see Wolff, 2006, for an extensive review). Although recent work has identified cutting-edge technologies for biological testing of substance use, *urinalysis* remains the preferred method of detection for several reasons. First, because urinalysis has been used historically, it is well-known and many of the problems associated with it have been addressed. Second, urine contains high concentrations of the target drug or its metabolites. Third, it is inexpensive and may be acquired in a minimally invasive manner as compared to other biological approaches. Self-contained urine-based testing kits that can reliably detect the most commonly used psychoactive substances are becoming increasingly available, which allow practitioners and researchers to

conduct on-site testing across a wide range of settings. Finally, recently developed quantitative and semi-quantitative tests are more sensitive to changes in the pattern, frequency, and amount of use (Preston, Silverman, Schuster, & Charles, 2002). Thus, in addition to indicating the presence or absence of a drug, quantitative urinalysis can be useful in detecting initial efforts to reduce drug use and monitoring the effects of treatments.

While urinalysis has several advantages and obvious clinical utility, several limitations remain. Urine can only indicate drug use in the past 3 days (except for cannabis, methadone, and diazepam), thereby increasing the reliance on self-report for longer-term follow-up periods. In addition, urine is easily adulterated by using chemicals such as bleach, vinegar, or liquid soap, and can be easily diluted by using old urine or someone else's urine. Conversely, over-the-counter medications and certain foods can produce positive test results in the absence of illicit drug use. As such, careful attention to detail and procedures are needed to ensure accurate collection, and positive tests may need additional confirmation.

Blood collection is another method that can detect very recent drug use and is considered an ideal method for assessing quantitative levels when accuracy is the primary criterion for measure selection. However, blood is often not collected due to its invasive nature, reliance on trained personnel, and the potential risk of spreading infections such as HIV and hepatitis. *Saliva* is the only body fluid that can be used as a substitute for blood, as drug concentration levels are comparable. Saliva collection has the advantage of being easy to obtain and is cost effective because, similar to urinalysis, self-contained testing kits are widely available that eliminate the need for trained personnel and off-site testing. One collection procedure often utilized is the sallivete-sampling device. It consists of a cotton wool swab, which is placed in the patients' buccal cavity for saliva collection by absorption. Drawbacks to saliva collection include difficulty collecting an adequate amount for drug detection and the possible contamination of the oral cavity as a result of oral, intranasal, and smoking drug use.

Hair testing has been developed and theorized to have the potential benefits of drug detection over a longer period of time as is not possible with the aforementioned methods. However, quality control criteria and standard laboratory methods have yet to be established. In addition, evidence indicates that drug detection may differentially appear in darker hair, leading to a bias toward missing drug use in blonde individuals and differentially detecting it in people with black hair. In addition, hair is sensitive to smoke in the air, resulting in a false positive for individuals who abstain yet are surrounded by people who have smoked drugs.

ETIOLOGICAL CONSIDERATIONS

BEHAVIORAL GENETICS AND MOLECULAR GENETICS

Behavioral Genetics Findings from twin, adoption, and family studies suggest that genetic factors account for a significant portion of the variance in liability for substance use disorders. Indeed, SUDs are some of the most highly heritable psychiatric disorders, with heritability estimates ranging from 0.39 for hallucinogens to 0.72

for cocaine (Goldman, Oroszi, & Ducci, 2005). The magnitude of genetic influence on substance use varies over the course of development, beginning with a negligible amount of genetic influence during early adolescence that increases over time until it stabilizes by age 35 to 40 (Kendler, Schmitt, Aggen, & Prescott, 2008). It also appears that the majority of the genetic vulnerability for SUDs can be accounted for by shared genetic influences that are common across drug classes (Agrawal, Neale, Prescott, & Kendler, 2004; True et al., 1999; Tsuang et al., 1998). For SUDs that are highly comorbid, such as alcohol and nicotine dependence, a common genetic factor for alcohol use and smoking accounts for approximately 45% of the genetic variance in heavy alcohol use and 35% of the genetic variance in heavy smoking (Swan, Carmelli, & Cardon, 1997). These findings point to significance of genetic factors in addiction liability, as well as the importance of studying genes that are involved in neurobiological substrates that are common across substance use disorders.

Molecular Genetics More recent work has focused on the extent to which specific genetic polymorphisms (variations in DNA structure) contribute to one's vulnerability for an SUD. The strongest and most consistent single-gene effects on SUD vulnerability are largely specific to Asian populations, including polymorphisms in the aldehyde (ALDH) and alcohol dehydrogenase (ADH) genes, which code for enzymes involved in alcohol metabolism (Wolff, 1972). Individuals who carry one or more of these alleles are less likely to become alcohol dependent (reviewed by Uhl, Drgon, Johnson, & Liu, 2009), and the protective effects of these genes appear to be additive (Thomasson et al., 1991).

Also significantly associated with substance dependence are γ-aminobutyric acid (GABA) receptor genes on chromosome 4. Convergent evidence suggests that polymorphisms, specifically in GABA2, are associated with alcohol dependence (Covault, Gelernter, Hesselbrock, Nellissery, & Kranzler, 2004; Edenberg et al., 2004; Fehr et al., 2006; Lappalainen et al., 2005; Soyka et al., 2008), nicotine dependence, cannabis use, and polysubstance abuse (Agrawal, Pergadia, Saccone, Hinrichs, et al., 2008; Agrawal, Pergadia, Saccone, Lynskey, et al., 2008; Drgon, D'Addario, & Uhl, 2006). Evidence from recent genome-wide association studies (GWAS) has converged to implicate a cluster of nicotinic acetylcholine receptor (nAChR) subunit genes in nicotine dependence, as well as dependence on other substances. For example, variants in CHRNA4 and the CHRNA5/A3/B4 cluster have been associated with nicotine dependence across populations, as well as subjective response to smoking (Berrettini et al., 2008; Feng et al., 2004; Hutchison et al., 2007; Li et al., 2005; Saccone et al., 2007; Weiss et al., 2008). Meta-analytic approaches have provided convergent evidence for the role of nAChR subunit genes, including CHRNA3 and CHRNA5, in smoking initiation and smoking quantity (Liu et al., 2010; Thorgeirsson et al., 2010; Tobacco and Genetics Consortium, 2010), alcohol dependence (Wang et al., 2009), and cocaine dependence (Grucza et al., 2008); however, the effect on cocaine dependence is opposite to that seen in nicotine dependence.

Additional genes that increase the risk of SUDs include polymorphisms in dopamine receptor genes that play a role in reward and reinforcement behavior (Blum et al., 2000). A meta-analysis including 55 studies confirmed the $A1^+$ allele of DRD2 as a

marker of substance use and severe substance misuse (Young, Lawford, Nutting, & Noble, 2004). Similarly, a polymorphism in the DAT1 gene has been associated with cocaine abuse (Guindalini et al., 2006) and alcohol dependence (Samochowiec et al., 2006). Recent meta-analyses provide additional support for the involvement of both genes in substance dependence across drug classes (reviewed by Li & Burmeister, 2009), suggesting that genes encoding for dopaminergic functioning may modulate SUD liability to a variety of substances.

Gene-Environment Interactions Beyond examining genetic factors in isolation, environmental risk factors have been shown to interact with genes to contribute to the development of SUDs. For example, individuals with the A1 allele of the DRD2 gene who also report high levels of stress are at the greatest risk of alcohol dependence (Bau, Almeida, & Hutz, 2000; Madrid, MacMurray, Lee, Anderson, & Comings, 2001). Similarly, Blomeyer and colleagues (2008) found that adolescents with the C allele of a single nucleotide polymorphism (SNP) in CHRNA1 were at an increased risk of alcohol use and heavy drinking, but only if they also experienced three or more negative life events. Additionally, polymorphisms in the monoamine oxidase A (MAOA) gene interact with childhood maltreatment in predicting alcohol use problems (Ducci et al., 2007; Nilsson et al., 2007; Nilsson, Wargelius, Sjöberg, Leppert, & Oreland, 2008). Related to smoking outcomes, one recent study found that an SNP in CHRNA5 increased the risk of nicotine dependence, but only among individuals who reported low levels of parental monitoring during early adolescence; however, parental monitoring did not moderate the effect of an SNP in CHRNA3 on nicotine dependence (Chen et al., 2009). Taken together, genetic risk factors for substance use may be moderated by environmental variables, suggesting that as genetic researchers continue to incorporate environmental measures into their studies, additional gene-environment interactions may be revealed.

NEUROANATOMY AND NEUROBIOLOGY

Several neurobiological models have been proposed to explain how chronic substance use contributes to development of SUDs and vulnerability to relapse, with a great deal of emphasis placed on the role of neuroadaptive changes that take place in brain reward and stress circuits over the course of chronic drug use (e.g., Koob & Le Moal, 2001, 2008; Li & Sinha, 2008; Robinson & Berridge, 1993, 2001; Wise, 1980, 2002). The following sections will discuss neurobiological mechanisms that increase liability to substance use across drug classes, as well as the neurobiological changes that contribute to development and maintenance of SUDs.

Brain Reward Circuits One pharmacological effect that is common to all drugs of abuse is increased activation in the mesocorticolimbic dopamine pathway of the brain (Di Chiara et al., 2004; Wise, 1996). Dopamine neurons project from the ventral tegmental area (VTA) to the ventral striatum and prefrontal cortex (PFC), and dopaminergic functioning in these regions is believed to be a key component of the brain reward systems, which are critical for the reinforcing properties of drugs. Human neuroimaging studies show that acute administration of nearly all drugs of abuse leads to increased activation in mesolimbic dopaminergic regions, and that this

activation correlates with subjective ratings of high or euphoria and craving. However, chronic drug administration and acute withdrawal are associated with alterations in this pathway, characterized by decreases in extracellular dopamine, reduced D2 receptor availability, and reduced dopamine transmission in frontal and ventral striatal regions (for detailed reviews, see Koob & Le Moal, 2008; Sinha, 2008; Volkow, Fowler, & Wang, 2002). Based on this evidence, some researchers have suggested that neuroadaptive changes that take place in dopaminergic circuits over the course of chronic drug use may underlie the aversive affective symptoms that are common during withdrawal, which may drive individuals to relapse to drug use in order to escape this aversive state (Koob & Le Moal, 1997, 2008). As such, alterations in dopaminergic functioning appears to be an important neurobiological mechanism underlying the development and maintenance of addictive disorders.

Brain Stress Circuits The hypothalamic-pituitary-adrenal (HPA) axis and its primary hormone, cortisol, plays a central role in mediating the body's response to stress and is extremely sensitive to inputs from the limbic system and prefrontal cortex, two brain areas that are important for modulating reinforcement and motivational processes (e.g., Li & Sinha, 2008). In animal models of substance use, evidence suggests that rats with elevated HPA axis reactivity to stress show greater self-administration of addictive substances (Piazza, Deminiere, Le Moal, & Simon, 1989, 1990; Piazza, Derouche, Rouge-Pont, & Le Moal, 1998; Piazza et al., 1991; Piazza et al., 1996), and administration of exogenous corticosteroids to rats that were low-level responders led to an increased risk that these rats would begin to self-administer amphetamines (Piazza et al., 1991). Evidence also suggests that HPA axis activation, and subsequent release of ACTH and cortisol in response to stress, is associated with increased dopaminergic neurotransmission in mesolimbic reward circuits (Dunn, 1988; Kalivas & Duffy, 1989; Piazza & Le Moal, 1996; Prasad, Sorg, Ulibarri, & Kalivas, 1995; Thierry, Tassin, Blanc, & Glowinski, 1976), suggesting that reactivity in brain stress circuits plays an important role in both substance use liability and drug reinforcement.

Neuroadaptation in Reward and Stress Circuitry Neurobiological models of drug addiction hypothesize that reward and stress circuits in the brain become dysregulated in response to chronic drug use, and this dysregulation contributes to the establishment of a "negative affect" or psychologically distressed state during abstinence, which increases the reinforcing effects of drugs and thus vulnerability to relapse following cessation (Koob, 2009; Koob & Le Moal, 2001, 2008). Specifically, when reward pathways (i.e., the mesocorticolimbic dopamine system discussed previously) are activated by drug administration, opposing antireward systems (i.e., brain stress systems localized in the central nucleus of the amygdala and the bed nucleus of the stria terminalis) are recruited to limit reward function and maintain homeostasis. Over the course of chronic drug administration, neuroadaptive changes occur in response to the excessive utilization of brain reward systems, including subsequent decreases in activation of brain reward systems and increases in the opposing brain stress circuits. Such combination of depressed reward circuits and elevated antireward circuits is hypothesized to be the driving force motivating continued drug-seeking behavior (Koob & Le Moal, 2008). Furthermore, elevated

brain stress activation is hypothesized to reduce an individual's ability to adapt to or cope with additional stressors during abstinence, thereby driving vulnerability to stress-induced relapse. This is in line with the negative reinforcement theory of addiction, which states that the motivation for substance use is the reduction or avoidance of negative emotional states (Baker, Piper, McCarthy, Majeskie, & Fiore, 2004). Indeed, evidence indicates that a behavioral proxy of negative reinforcement, namely distress tolerance, is associated with an increased frequency of substance use and poor substance use outcomes (Brandon et al., 2003; Brown, Lejuez, Kahler, & Strong, 2002; Daughters, Lejuez, Bornovalova, et al., 2005; Daughters, Lejuez, Kahler, Strong, & Brown, 2005; Quinn, Brandon, & Copeland, 1996). Taken together, neurobiological models suggest that chronic drug use is associated with neuroadaptive changes, including decreases in reward system activation and increases in antireward system functioning, which may serve to maintain compulsive drug-seeking behaviors, even after protracted periods of abstinence.

LEARNING, MODELING, AND LIFE EVENTS

Theories of learning and conditioning have been utilized to understand the development and maintenance of SUDs, and as a result, studies have been conducted in laboratory animals and humans that support the notion of drugs as reinforcers (for a review, see Higgins, Heil, & Lussier, 2004), with drug use theorized to be a form of operant behavior influenced by antecedents and consequences. Drug self-administration studies with humans have been used to examine the influence of nondrug reinforcers on heroin and cocaine use (Comer, Collins, & Fischman, 1997; Greenwald & Steinmiller, 2009; Higgins et al., 1994). In each study, the choice of using either cocaine or heroin decreased in an orderly and graded function of increasing value of a monetary option. Specifically, as the nondrug reinforcer increased in value, drug use decreased, suggesting the power of alternative reinforcers in affecting drug use.

Taking this approach a step further, the behavioral economics perspective proposes that the reinforcing value of drug use is critically influenced by the environmental context of other available reinforcers. Accordingly, research has revealed a relationship between degree of substance use and engagement in substance-free activities. High rates of drug use are most likely in contexts without substance-free sources of reinforcement, and drug use will generally decrease if access to alternative reinforcers is increased (Higgins, Heil, & Lussier, 2004). In a comprehensive review of the literature, Carroll (1996) concludes that the availability of nondrug alternative reinforcers reliably reduces drug use in animals and humans across a variety of drug types, routes of administration, and types of alternative reinforcers. Although the majority of research in this area has focused on alcohol use (e.g., Correia, Benson, & Carey, 2005), findings have also been demonstrated among illicit drug users (Van Etten, Higgins, & Budney, 1998). Taken together, individuals with fewer alternative behavioral choices will be more likely to develop an SUD. Additionally, clinical research has reported positive outcomes for treatments developed based upon reinforcement theories such as contingency management (e.g., Prendergast, Podus, Finney, Greenwell, & Roll, 2006), behavioral activation (Daughters et al., 2008), and a community reinforcement approach (e.g., Abbott, 2009).

In addition to behavioral theories of addiction, research has evidenced an association between stressful life events and substance use. Chronic stress has been identified as a contributor to both substance use initiation and maintenance (Fox & Sinha, 2009). Adolescent exposure to stressful life events, such as parental alcoholism or financial difficulty, has been shown to increase emotional and behavioral problems that intensify the risk for developing an SUD (King & Chassin, 2007). Furthermore, populations dealing with chronic stress, including emotional stressors ranging from violence and loss to trauma, poor social support, and interpersonal conflict, have evidenced higher vulnerability to SUDs (Sinha, 2008).

Cognitive Influences

Expectancies Turning to research emphasizing the role of cognition, social learning theories (Bandura, 1977) emphasize the role of a biased belief system in maintaining substance use. These theories posit that positive expectancies for engaging in drug use, coupled with minimal negative expectancies, and poor self-efficacy beliefs as to one's ability to cope without drugs, leads to the development and maintenance of SUDs. Specifically, substance use expectancies are an individual's beliefs about the consequences of substance use (e.g., "I expect to feel good if I use marijuana"). The beliefs and attitudes that drive substance use expectancies are generated from a range of sources, such as the perception of use, actual experiences, social norms, and peer influence (Hayaki et al., 2010). Empirical evidence indicates that there is a relationship between positive expectancies and substance use (McCusker, 2001). For example, in a community sample of cocaine users, the expectation that use would increase physical and social pleasure was positively associated with frequency of cocaine use (Hayaki, Anderson, & Stein, 2008). Furthermore, positive expectancies have predicted the initiation and maintenance of alcohol consumption, the onset of drinking problems, and in some studies, emergence and persistence of alcohol dependence (Jones, Corbin, & Fromme, 2001). Conversely, research has also highlighted the role of negative expectancies, particularly as a predictive tool for continued abstinence following treatment (McCusker, 2001). Negative expectancies (e.g., "If I drink alcohol, I will lose control") also act as motivation to limit substance use (Oei & Morawska, 2004).

Executive Functioning Executive functioning is implicated in behavior regulation and control, and includes the constructs of impulsivity, decision making, and attentional bias. Across studies, impulsivity has been associated with the initiation and continued use of substances (de Wit, 2009; Field, Schoenmakers, & Wiers, 2008; Johnson, Bickel, Moore, Badger, & Budney, 2010; Petry & Casarella, 1999). Drug use also causes neuronal changes that alter a person's ability to choose nonrisky alternative behaviors, though others argue that the decision-making mechanism is already weak in individuals who are prone to addiction (Bechara, 2005). For instance, using the Game of Dice Task (Brand et al., 2004), Brand and colleagues (2008) found subjects with opiate dependence exhibited a preference for decisions that led to more negative long-term consequences and made riskier choices compared to matched controls (Brand, Roth-Bauer, Driessen & Markowitsch, 2008). The relationship between attentional bias and SUDs has demonstrated that illicit drug users attend more to drug-related

stimuli (Costantinou et al., 2010; Hester, Dixon, & Garavan, 2006; McCusker & Gettings, 1997), and a stronger attentional bias is associated with heavier substance use (Stacey & Wiers, 2010).

Sex and Racial-Ethnic Considerations

Sex Differences Existing research has demonstrated that women differ from men in their pathways into drug addiction. Compared to men, women are less likely to have an SUD, and onset of their substance abuse tends to be later in life. Yet women become dependent at a quicker rate and experience more severe consequences of drug use over shorter periods of time (e.g., Hser, Huang, Teruya, & Anglin, 2004). This accelerated development to dependence has been termed *telescoping*, and this trend has been consistently documented (Greenfield, Back, Lawson, & Brady, 2010). For women the pathway into drug use is often relationship-based; for instance, women are more likely to initiate and continue substance use in the context of an intimate partner relationship (Frajzyngier et al., 2007; Tuchman, 2010), and following treatment, women's drug use is more likely to be influenced by their partners' continued substance use, compared to men (Grella, Scott, Foss, & Dennis, 2008). Furthermore, women with SUDs are also more likely than men with SUDs to have a partner who uses illegal drugs (Westermeyer & Boedicker, 2000).

With regard to treatment, co-occurring psychiatric disorders are more common among women and also create a barrier to treatment. As indicated in a review by Greenfield and colleagues (2007), females have higher rates of SUDs and specifically eating disorders, mood and anxiety disorders, and posttraumatic stress disorder, which subsequently make it difficult for them to find appropriate treatment to manage both disorders. Gender differences in stress reactivity may be one important mechanism underlying these differences. Fox and Sinha (2009), in a review, reported that compared to substance-abusing men, women may experience increased emotional sensitivity to changes in the stress system, and the resulting neuroadaptations in autonomic function and affect may alter vulnerability to co-occurring disorders, possible relapse, and treatment outcome.

Women also face unique barriers to treatment engagement that may explain women's reduced likelihood to enter treatment relative to men. For instance, barriers relating to child-rearing responsibilities, including limited access to child care services, as well as society's punitive attitude toward substance abuse by women as child bearers, present just some of the major treatment barriers for women suffering from SUDs (e.g., Greenfield et al., 2007). Moreover, women also differ from men in their response to treatment. Data on this topic have proven to be somewhat conflicting: Whereas some researchers have reported that women are more likely than men to drop out of substance abuse treatment (King & Canada, 2004), others have proposed a complex interaction of gender and treatment modality (e.g., methadone versus drug-free programs; Joe, Simpson, & Broome, 1999; McCaul, Svikis, & Moore, 2001; Simpson, Joe, Rowan-Szal, & Greener, 1997). There is also evidence that women are more likely than men to complete treatment (Hser et al., 2004). The reasons underlying these discrepancies are unknown, but they suggest a fruitful avenue for future research.

Racial-Ethnic Differences Studies suggest that there are unique risks and needs among minority drug users. For instance, racial-ethnic minorities who reside in inner-city areas are particularly vulnerable to drug use and risky sexual behavior as a result of higher levels of poverty, violence, general risk practices, and availability of street drugs (e.g., Avants, Marcotte, Arnold, & Margolin, 2003). Importantly, there are great racial-ethnic disparities in access and utilization of treatment services, and evaluations of the substance abuse treatment system have shown that racial-ethnic minorities are underserved (Marsh, Cao, Guerro, & Shin, 2009). Aside from Asian Americans, all racial groups have a larger treatment gap than Whites (Schmidt & Mulia, 2009), and among treatment-seeking individuals, African Americans and Hispanics are more likely than Whites to report unmet needs (Wells, Klap, Koike, & Sherbourne, 2001).

As with other health care access issues, racial-ethnic differences in accessing substance abuse treatment services may result from underlying differences in barriers to care. Factors such as perceived discrimination, prior negative experiences associated with services, and limited knowledge of available services may provide a better understanding of why there is an unmet need among those who perceive need for substance abuse treatment in minority groups (Grella, Karno, Warda, Moore, & Niv, 2009), and data indicate that Whites experience half the rate of barriers compared to African Americans and Hispanics (Perron et al., 2009). Looking beyond access and utilization of treatment, treatment outcome studies suggest mixed findings when exploring racial-ethnic minorities compared to Whites. Some data indicate that members of minority groups are less likely to complete and/or seek treatment, receive fewer treatment services, and are less likely to achieve recovery (Jerrell & Wilson, 1997; Rebach, 1992). However, research reports indicate that minority clients do not differ from nonminority clients in their response to treatment (e.g., Pickens & Fletcher, 1991) and in treatment outcomes (Niv, Pham, & Hser, 2009).

COURSE AND PROGNOSIS

By the 12th grade, more than 47% of adolescents have used an illicit substance (Johnston, O'Malley, Bachman, & Schulenberg, 2009). The most common substances used by adolescents include tobacco, cannabis, and alcohol (SAMHSA, 2009a). It should be noted that although many adolescents may experiment with drugs, most do not progress to abuse or dependence (Newcomb & Richardson, 1995). There is an ongoing debate about the development and progression of substance use among adolescents. Some researchers subscribe to the "gateway theory," which hypothesizes that for adolescents, there is a distinct sequential pattern of substance use, beginning with licit substances (i.e., tobacco, alcohol) and progressing to illicit substance (e.g., marijuana), and finally advancing through a hierarchy of illicit substances (e.g., cocaine, heroin; Kandel, Yamaguchi, & Chen, 1992). However, more recent research finds that adolescent substance use does not always evidence a temporal sequence from licit to illicit substances, and the choice of substance used by adolescents is a function of contextual variables (e.g., availability, parental supervision) more than a normative sequential order (Tarter, Vanyukov, Kirisci, Reynolds, & Clark, 2006).

Although there are conflicting hypotheses as to adolescent use and progression, research has consistently evidenced similar risk factors for the development of

substance dependence. Two primary risk factors include age of initiation and frequency of use during adolescence (Behrendt, Wittchen, Hofler, Lieb, & Beesdo, 2009; Degenhardt et al., 2009; King & Chassin, 2007). Age of initiation increases risk in part because earlier age of substance use allows for greater exposure to the substance. Considering that adolescence is a time of substantial neurological development, the adolescent brain may be particularly susceptible to substance abuse and addiction (Winters & Lee, 2008). In addition, drug-related problems (i.e., some symptoms of an SUD without meeting full diagnostic criteria) in adolescence significantly predict a future SUD, elevated levels of depression, and antisocial and borderline personality disorder symptoms by age 24 (Rohde, Lewinsohn, Kahler, Seeley, & Brown, 2001).

Once an SUD is present, recovery is notoriously difficult, even with exceptional treatment resources. For those who receive treatment, the next challenge is staying in treatment. Treatment dropout rates range up to 50% (SAMHSA, 2007). Such high rates of premature treatment termination are of concern, because time in treatment is related to positive outcomes (e.g., Garner, Godley, Funk, Lee, & Garnick, 2010; Simpson, Joe, & Brown, 1997). As for relapse rates, estimates suggest that 90% of heroin- and cocaine-dependent users experience at least one relapse within 4 years after treatment, with many relapsing considerably sooner. Furthermore, of the patients admitted to the U.S. public treatment system in 2007, approximately 57% were re-entering treatment (Office of Applied Studies, 2009). Retrospective and prospective treatment studies report that most participants initiate three to four episodes of treatment over multiple years before attaining abstinence (Hser, Maglione, Polinksy, & Anglin, 1998), and as many as 80% transition between treatment, recovery, using, and incarceration at least once over a 4-year follow-up period (Grella et al., 2008).

Treatment outcomes are dependent on a variety of factors, including individual characteristics and life problems, severity of addiction and drug use, aptness of treatment and linkage to services to treat other problems, and the quality of the transaction between the individual and the treatment program (NIDA, 2009). As previously stated, better treatment outcomes are related to length of stay, and for residential/inpatient and outpatient programs, treatment participation of 90 days or longer is recommended for sustaining recovery and positive results (NIDA, 2009). However, 90 days of treatment is not always feasible (i.e., lack of insurance and prohibitive cost). Historically, persons with SUDs receive a traditional acute treatment approach involving assessment, treatment, and discharge all within a short time frame (i.e., 28 days or 2 months), with the supposition that the patient is cured and will be able to maintain abstinence following the single treatment episode (Dennis & Scott, 2007).

However, recent literature addresses SUDs as a chronic condition, analogous to other chronic medical diseases. For example, McLellan and colleagues (McLellan, Lewis, O'Brien, & Kleber, 2000) illustrate the similarities in genetic heritability, environmental factors, and personal choice within addiction and other medical conditions with chronic care treatment (e.g., type 2 diabetes mellitus, hypertension, and asthma). Of note, they found that treatment compliance for individuals with an SUD is no better than adherence rates to prescribed treatments for these other medically accepted chronic diseases (McLellan et al., 2000). Similar to chronic diseases such as diabetes and congestive heart failure, there is no cure for addiction and multiple relapses are common (Saitz, Larson, LaBelle, Richardson, & Samet, 2008);

therefore, adjusting treatment to involve a continuum of care may improve long-term outcomes for people with SUDs.

CASE STUDY

Case Identification

The patient (John) is a 45-year-old African American male who entered treatment voluntarily at an urban residential substance use treatment center.

Presenting Complaints

John reports that he relapsed to substance use 8 months ago, and his primary drug of choice is crack/cocaine accompanied by frequent alcohol use. He reports that he had success in treatment for the first time after he was released from prison 4 years ago, and he would like to try and get back on track, as he has hit a low point in the past few months. At the time of treatment entry, John reports no stable living arrangement and had recently been splitting time at the homes of his friends, ex-girlfriend, and uncle. He has four children between the ages of 10 and 27, with three separate women, and has intermittent contact with each of them. He reports that a fifth child, his oldest son, was murdered 5 months ago in a drug-related incident. In his current environment, he reports spending most of his time with old friends, who he reestablished a relationship with after he was laid off from his job 9 months ago.

History

John was raised by his mother and never met his father. He reports an extensive family history of substance use, including heroin and crack/cocaine use in his mother, who passed away 10 years ago. John dropped out of high school after the 10th grade. Between the ages of 18 and 40, he was arrested and spent time in prison multiple times for charges related to theft and possession of cocaine. He was released from his last prison term at the age of 41. He has worked primarily as an assistant electrician over the course of his life, but he refused to provide additional details regarding his employment history. His most stable employment history has been during the past 4 years after completing a court-mandated treatment at a residential substance use treatment facility. He reports that he was committed to "turning my life around" at this time, and he successfully remained abstinent until approximately 6 months ago.

Assessment

The Addiction Severity Index and a clinical interview for *DSM-5* were administered to determine existing psychopathology, including substance dependence, substance use history and severity, environmental strengths and stressors, legal issues, and psychiatric symptoms. During the interview, John displayed psychomotor retardation, clear thought processes, and no obvious perceptual abnormalities. His speech volume and tone were within normal limits, yet his speech rate was somewhat slower than normal. Based on this assessment, John met criteria for current crack/cocaine dependence (severe), current alcohol dependence (mild), and major depressive disorder (MDD).

He reported past crack/cocaine and alcohol dependence beginning at age 17. His MDD symptoms include depressed mood most of the day, nearly every day, markedly diminished interest in almost all activities, feelings of worthlessness and excessive guilt, and a diminished ability to think or concentrate. After a careful assessment of the timeline of his symptoms, it was concluded that his MDD is not substance induced, as his symptoms preceded the onset of his relapse to substance use. They also preceded the death of his son and are therefore not solely a product of grief.

The assessment of legal issues indicated that he is no longer on probation with the court system and entered treatment voluntarily. John evidenced difficulty in identifying strengths, but with some additional probing he was able to acknowledge potential support from his uncle and sister, as well as the importance of his spirituality. He reports that his Narcotics Anonymous (NA) sponsor was a source of support but moved away from the area about a year ago. He stopped attending NA meetings around that time.

It was determined that a functional analysis to identify the antecedents and consequences of his substance use and depression would provide the most useful information for treatment planning. First, following the loss of his job, he reported that he had a lot of free time and got bored easily. He felt worthless that he couldn't find a job and often ruminated over the guilt he felt about his choices in life and his inability to provide for his family. He contacted his old friends, which was soon followed by cocaine and alcohol use. He also reported feeling lonely, guilty, and worthless following the loss of his son, and drug use helped him "get rid of" these feelings, although they would always resurface when he was sober, leading to a cycle of negative reinforcement. Finally, he reported intensifying feelings of sadness and shame that he had used crack/cocaine and alcohol again given how much progress he had made following his release from prison. He felt that he had let his family down, as he was just starting to reestablish relationships with his children before his relapse. Taken together, it appeared that a lack of drug-free reinforcements following loss of his job was strongly associated with his relapse to substance use. This was soon thereafter compounded by the negative feelings about the loss of his son, leading to substance dependence and a cycle of negative reinforcement.

SUMMARY

Substance use problems are complex, and a comprehensive understanding requires knowledge of biological, genetic, neural, behavioral, and cognitive factors. This chapter provides an overview of current practices and cutting-edge advancements for understanding and assessing drug-specific SUDs. Although much work is still needed, great progress has been made in understanding development of SUDs, with greatest promise evident in approaches that consider the interactive influence of these factors. Additionally, clear advancements have been made in both initial as well as ongoing assessment using self-report, interview, behavioral, and biological methods. Also of great promise is the greater attention to neurobiological, genetic, gender, and diversity issues when considering vulnerabilities to developing SUDs, as well as barriers to assessment and proper treatment. In summary, although the challenges of understanding and assessing SUDs remain, it is clear that the field has evidenced important advancements aimed at addressing these challenges.

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CHAPTER 19

Neurocognitive Disorders

GERALD GOLDSTEIN

INTRODUCTION AND RECENT DEVELOPMENTS

Most neurological disorders are ancient diseases, and developments in treatment and cure have been painfully slow. However, we continue to learn more about these disorders, and in previous versions of this chapter (Goldstein, 1997, 2007) we highlighted substantive developments. A new disorder, AIDS dementia, had appeared, and the marker for the Huntington's disease gene had been discovered. At the time of the 1997 writing, it was mentioned that a still mysterious and controversial disorder appeared, sustained by military personnel during the war with Iraq in the Persian Gulf area, popularly known as the Gulf War syndrome. An aspect of this syndrome has been said to involve impaired brain function (Goldstein, 2011; Goldstein, Beers, Morrow, Shemansky, & Steinhauer, 1996). A more readily understood condition emerging from the recent Iraq and Afghanistan Wars is the blast injuries caused largely by roadside bombs. These injuries appeared to have different characteristics from those associated with the open or closed head injuries associated with previous wars and accidents in civilian life (Belanger, Kretzmer, Vanderploeg, & French, 2010).

Another consequence of the Iraq and Afghanistan Wars has been a reconsideration of the problem of mild traumatic brain injury (mTBI), often called concussion. Concussion is a common sports injury, but it also appears to be a common consequence of sustaining a blast injury. It is sometimes complicated by its association with posttraumatic stress disorder (PTSD) acquired in reaction to the injury, and diagnostic difficulties have been created regarding whether the victim sustained brain injury, developed PTSD, or both. It was commonly accepted that concussion was a self-limiting disorder, and that essentially full recovery could be expected within no more than 90 days. Recently, however, it has been observed that some individuals with histories of concussion do not fully recover and continue to have complaints of cognitive problems, notably in attention, memory, and organizational abilities. Individuals with multiple concussions appear to experience a cumulative effect.

Initially, these symptoms were attributed to stress, but neuroimaging studies using advanced technologies have found that identifiable brain damage may result from concussion, involving the upper brainstem, base of the frontal lobe, hypothalamic-pituitary axis, medial temporal lobe, fornix, and corpus callosum. Bigler

(2008) has written a review of this area, using the phrase "persistent postconcussive syndrome" to describe this condition. Substantial support for the neurological basis for this disorder comes from use of a technology that was just beginning its development and widespread use at the last writing, called diffusion tensor imaging (DTI). DTI is an MRI-related procedure that tracks axonal white matter, identifying misalignments.

In the Gulf War, concussion and more serious trauma was associated with blast injuries sustained mainly as a result of roadside bombing. Blast injuries remain a controversial area, with some authorities claiming they are no different from the commonly accepted types of brain injury (Hoge et al., 2008; Wilk et al., 2010), but with others claiming they are a unique form of trauma not identified previously. The matter is further complicated by the fact that the bombs used were sometimes loaded with depleted uranium or possibly infectious agents. Thus, the understanding of head injury has changed since the last writing, with the development of methods that can detect persistent neurological consequences of concussion producing a new diagnosis called persistent postconcussive syndrome, and the problem of blast injury, which is still under intensive investigation.

DIAGNOSTIC CONSIDERATIONS

With the publication of *DSM-5*, there are substantial changes from *DSM-IV* in terminology and content. The name of the category "Delirium, Dementia, Amnestic, and Other Cognitive Disorders" has been replaced by the phrase "Neurocognitive Disorders." The term *delirium* remains as part of a set of three major subcategories: Major Neurocognitive Disorder, Minor Neurocognitive Disorder, and Delirium. The term *dementia* has been eliminated.

It may be useful to review the rationale for the changes made in *DSM-5*. The DSM-5 Neurocognitive Disorders Work Group prepared a document that contains their proposals for changes and their rationales for proposing them (American Psychiatric Association, 2010). We summarize some of their major points here:

1. Efforts were made to eliminate demeaning or stigmatizing terminology. Just as the term *mental retardation* has been replaced by *intellectual disability* in the Neurodevelopmental Disorders section, the term *dementia* has been replaced by *Major and Mild Neurocognitive Disorders*. These new terms are felt to reflect more accurately the nature of the disorder and a general attempt made by the writers of *DSM-5* to correct for the demeaning, stigmatizing connotations of the names of some psychiatric disorders. The change from *mental retardation* to *intellectual disability* has already been widely accepted.
2. Diagnostic criteria wording was changed to increase precision. Thus, for example, the term *consciousness* has been changed to *level of awareness*. The changes in cognition specified in *DSM-IV* mention only memory, orientation, and language. In *DSM-5* the domains of executive ability and visuospatial impairment are also specified.
3. Mention of severity is added to characterize development of a disturbance.
4. Specific symptoms of delirium are provided, such as hallucinations, delusions, and sleep-wake cycle disturbances.

5. Delirium is subcategorized into hyperactive, hypoactive, and mixed groups, again providing greater specificity.

6. There is a major reconceptualization regarding characterization of cognitive changes. The term *cognitive decline* replaces *cognitive deficits* to emphasize that major cognitive disorder is acquired and reflects a decline from previous level of performance. The previous model, based on Alzheimer's disease, requires that memory impairment must be present. However, data now indicate that in other neurocognitive disorders, other domains such as language or executive functions may be impaired first, and most prominently. The changed wording calls for decline from previous performance in one or more specified domains including memory, but also language (aphasia), disturbances of skilled movement (apraxia) or of recognition (agnosia) and executive function.

7. Emphasis is placed on objective assessment of performance that may include neuropsychological testing.

8. Emphasis is placed on independent performance of instrumental activities of daily living.

There have been changes in the number and description of the neurocognitive disorders. Dementia of the Alzheimer type has been renamed major or mild neurocognitive disorder due to Alzheimer's disease. The term *vascular dementia* has been replaced with *major* or *mild vascular neurocognitive disorder*. Other neurocognitive disorders/diagnoses now include frontotemporal, Lewy bodies disease, Huntington's disease, Parkinson's disease, traumatic brain injury, substance/medication use, HIV infection, and prion disease Neurocognitive Disorders, each of which can be modified by a major or mild descriptor (see clinical presentation section).

The diagnosis of mild neurocognitive disorder is new to the *DSM* system. The distinction is a matter of severity. Cognitive decline is characterized as modest or mild, it should not interfere with capacity for independence in everyday living, and delirium or another mental disorder can make a better explanation of the condition. This change allows for the diagnosis of less disabling syndromes that may still benefit from treatment.

In general, the changes in *DSM-5* have gone in the direction of increased specificity including more detailed documentation of symptoms, description of cognitive domains involved, providing an etiological diagnosis, consideration of subtypes and use of more precise terminology. The distinction between major and mild disorders allows for diagnosis of individuals with mild impairment who would not meet criteria for a diagnosable neurological disorder, but who have experienced cognitive decline associated with brain dysfunction that would benefit from programs of treatment and management, such as cognitive rehabilitation.

CLINICAL PRESENTATION

The theoretical approach taken here will be neuropsychological in orientation, and based on the assumption that clinical problems associated with brain damage can be understood best in the context of the relationship between brain function and behavior. Thus, we expand our presentation beyond the descriptive psychopathology of *DSM-5* (APA, 2013) in order to provide some material related to basic

brain-behavior mechanisms. There are many sources of brain dysfunction, and the nature of the source has a great deal to do with determining behavioral consequences: morbidity and mortality. Thus, understanding key neuropathological processes is crucial to understanding the differential consequences of brain damage, and in turn, that requires understanding how the brain functions, and in some cases the genetics and neurochemistry of how memories and other cognitive abilities are preserved in brain tissue.

In recent years, knowledge of the neurological systems important for such areas as memory and language has been substantially expanded. It seems clear now that there are several separate memory systems located in different areas of the brain, notably the hippocampus, the amygdala, the neocortex, and the cerebellum. Each system interacts with the others but supports a different form of memory, such as immediate recall, remote recall, and the brief storage of information during ongoing cognitive activity known as working memory (Baddeley, 1986).

Initially, two major methodologies were used to assess brain dysfunction: direct investigations of brain function through lesion generation or brain stimulation in animal subjects, and studies of patients who had sustained brain damage, particularly localized brain damage. The latter method can be dated back to 1861 when Paul Broca produced his case report (1861) on a patient who had suddenly developed speech loss. An autopsy revealed that he had sustained an extensive infarct in the area of the third frontal convolution of the left cerebral hemisphere. Thus, an important center in the brain for speech had been discovered, but perhaps more significantly, this case produced what many would view as the first reported example of a neuropsychological or brain-behavior relationship in a human. Indeed, to this day, the third frontal convolution of the left hemisphere is known as Broca's area, and the type of speech impairment demonstrated by the patient is known as Broca's aphasia.

Following Broca's discovery, much effort was devoted to relating specific behaviors to discrete areas of the brain. These early neuropsychological investigations not only provided data concerning specific brain-behavior relationships, but also explicitly or implicitly evolved a theory of brain function, now commonly known as classical localization theory. In essence, the brain was viewed as consisting of centers for various functions connected by neural pathways. In human subjects, the presence of these centers and pathways was documented through studies of individuals who had sustained damage to either a center or the connecting links between one center and another such that they became disconnected. To this day, the behavioral consequences of this latter kind of tissue destruction are referred to as a disconnection syndrome (Geschwind, 1965). For example, there are patients who can speak and understand, but who cannot repeat what was just said to them. In such cases, it is postulated that there is a disconnection between the speech and auditory comprehension centers.

Not all investigators advocated localization theory. The alternative view is that the brain functions as a whole in an integrated manner, currently known as mass action, holistic, or organismic theories of brain function. In contemporary neuropsychology the strongest advocates of holistic theory were Kurt Goldstein, Martin Scheerer, and Heinz Werner. Goldstein and Scheerer (1941) are best known for their distinction between abstract and concrete behavior, their description of the "abstract attitude," and the tests they devised to study abstract and concrete functioning in

brain-damaged patients. Their major proposition was that many of the symptoms of brain damage could be viewed not as specific manifestations of damage to centers or connecting pathways but as some form of impairment of the abstract attitude. The abstract attitude is not localized in any region of the brain but depends upon the functional integrity of the brain as a whole. Goldstein (1959) describes the abstract attitude as the capacity to transcend immediate sensory impressions and consider situations from a conceptual standpoint. Generally, it is viewed as underlying such functions as planning, forming intentions, developing concepts, and separating ourselves from immediate sensory experience.

The notion of a nonlocalized generalized deficit underlying many of the specific behavioral phenomena associated with brain damage has survived to some extent in contemporary neuropsychology, but in a greatly modified form. Similarly, some aspects of classical localization theory are still with us, but also with major changes (Mesulam, 1985). None of the current theories accepts the view that there is no localization of function in the brain, and correspondingly, none of them would deny that some behaviors cannot be localized to some structure or group of structures. This synthesis is reflected in several modern concepts of brain function, the most explicit one probably being that of Luria (1973). Luria has developed the concept of functional systems as an alternative to both strict localization and mass action theories. Basically, a functional system consists of several elements involved in the mediation of some complex behavior. For example, there may be a functional system for auditory comprehension of language. Thus, no structure in the brain is only involved in a single function. Depending upon varying conditions, the same structure may play a role in several functional systems. With regard to clinical neuropsychology, the main point is that there are both specific and nonspecific effects of brain damage. Evidence for this point of view has been presented most clearly by Teuber and his associates (Teuber, 1959) and by Satz (1966). The Teuber group was able to show that patients with penetrating brain wounds that produced very focal damage had symptoms that could be directly attributed to the lesion site, but they also had other symptoms that were shared by all patients studied, regardless of their specific lesion sites.

An old principle of brain function in higher organisms that has held up well and that is commonly employed in clinical neuropsychology involves contralateral control; the right half of the brain controls the left side of the body and vice versa. The contralateral control principle is important for clinical neuropsychology because it explains why patients with damage to one side of the brain may become paralyzed only on the opposite side of their body or may develop sensory disturbances on that side. We see this condition most commonly in individuals who have had strokes, but it is also seen in some patients who have open head injuries or who have brain tumors.

Although aphasia, or impaired communicative abilities as a result of brain damage, was recognized before Broca (Benton & Joynt, 1960), it was not recognized that it was associated with destruction of a particular area of one side of the brain. Thus, the basic significance of Broca's discovery was not the discovery of aphasia, but of cerebral dominance. Cerebral dominance is the term that has been commonly employed to denote the fact that the human brain has a hemisphere that is dominant for language and a nondominant hemisphere. In most people, the left hemisphere is dominant, and left hemisphere brain damage may lead to aphasia. However, some individuals have dominant right hemispheres, while others do not appear to have a dominant

hemisphere. Although why most people are left-hemisphere dominant remains unknown, what is clear is that for individuals who sustain left hemisphere brain damage, aphasia is a common symptom, while aphasia is a rare consequence of damage to the right hemisphere.

Following Broca's discovery, other neuroscientists discovered that just as the left hemisphere has specialized function in the area of language, the right hemisphere also has its own specialized functions. These functions seem to relate to nonverbal abilities such as visual-spatial skills, perception of complex visual configurations, and, to some extent, appreciation of nonverbal auditory stimuli such as music. Some investigators have conceptualized the problem in terms of sequential as opposed to simultaneous abilities. The left hemisphere is said to deal with material in a sequential, analytic manner, while the right hemisphere functions more as a detector of patterns or configurations (Dean, 1986). Thus, while patients with left hemisphere brain damage tend to have difficulty with language and other activities that involve sequencing, patients with right hemisphere brain damage have difficulties with such tasks as copying figures and producing constructions, because such tasks involve either perception or synthesis of patterns. In view of these findings regarding specialized functions of the right hemisphere, many neuropsychologists now prefer to use the expression functional asymmetries of the cerebral hemispheres rather than cerebral dominance.

With this basic brain-behavior background in mind, we now turn to a clinical description of the individual disorders that are included in the broad diagnostic category of Neurocognitive Disorders. This includes delirium and a number of individual disorders included under the major categories of major or mild neurocognitive disorders.

DELIRIUM

The first disorder listed in the *DSM-5* is delirium. This temporary condition is basically a loss of capacity to maintain attention with corresponding reduced awareness of the environment. Tremors and lethargy may be accompanying symptoms. Delirium is reversible in most cases but may evolve into a permanent neurocognitive or other neurological disorder. *DSM-5* allows for the specification of the cause of delirium, whether it is due to substance intoxication, substance withdrawal, medication-induced delirium due to another medical condition, or delirium due to multiple etiologies. Typically, delirium is an acute phenomenon and does not persist beyond a matter of days. However, delirium, notably when it is associated with alcohol abuse, may eventually evolve into permanent disorders in the form of a persistent neurocognitive disorder (formerly dementia). The behavioral correlates of delirium generally involve personality changes such as euphoria, agitation, anxiety, hallucinations, and depersonalization.

MAJOR AND MILD NEUROCOGNITIVE DISORDERS

There are several types of neurocognitive disorders, but they all involve usually slowly progressive deterioration of intellectual function. The deterioration is frequently patterned, with loss of memory generally being the first function to decline,

and other abilities deteriorating at later stages of the illness. As noted in *DSM-5*, the term *major* or *mild neurocognitive disorder* replaces the term *dementia* in an effort to eliminate stigmatization. The *DSM-5* approach to the diagnosis of the major and mild neurocognitive disorders is that there is first a determination of whether the individual is suffering from a major or mild type of cognitive impairment, and then the reason for the impairment is added (e.g., due to Alzheimer's disease) to indicate the distinct behavioral features and likely etiology. Furthermore, for either the major or mild types, there are "probable" or "possible" specifiers depending upon the strength of the evidence for the etiological factor (genetics, neuroimaging).

Major or Mild Neurocognitive Disorders of the Alzheimer's Type One class of neurocognitive disorders, major or mild neurocognitive disorder of the Alzheimer's type, arises most commonly in late life, either during late middle age or old age, although it may occur at any age. In children it is differentiated from intellectual disability on the basis of the presence of deterioration from a formerly higher level. These disorders are defined as those conditions in which, for no exogenous reason, the brain begins to deteriorate and continues to do so until death. As indicated in the psychological and biological assessment section, a diagnostic method has recently become available to specifically diagnose Alzheimer's disease in the living patient. Its presence also becomes apparent on examination of the brain at autopsy.

Clinically, the course of the Alzheimer's type generally begins with signs of impairment of memory for recent events, followed by deficits in judgment, visual-spatial skills, and language. The language deficit has become a matter of particular interest, perhaps because the communicative difficulties of patients with major or mild neurocognitive disorders of the Alzheimer's type are becoming increasingly recognized. Generally, the language difficulty does not resemble aphasia, but can perhaps be best characterized as an impoverishment of speech, with word-finding difficulties and progressive inability to produce extended and comprehensible narrative speech as illustrated in the descriptive writing of Alzheimer's disease patients (Neils, Boller, Gerdeman, & Cole, 1989). The patients wrote shorter descriptive paragraphs than did age-matched controls, and they also made more handwriting errors of various types. The end state is generalized, severe intellectual impairment involving all areas, with the patient sometimes surviving for various lengths of time in a persistent vegetative state.

Criteria for the Alzheimer's disease subtype include meeting criteria for major or minor neurocognitive disorder, early and prominent impairment in memory, deficits in at least one other domain in the case of the major form of the disorder, a course of gradual onset and continuing cognitive decline, and a ruling out of the condition being attributable to other disorders (APA, 2013). The diagnosis may indicate whether it occurs with or without behavioral disturbance. Separate criteria for psychosis and depression have been written.

Major or Mild Frontotemporal Neurocognitive Disorder In this disorder, there is specific impairment of social judgment, decision making, and particular language and memory skills. The decline in language can take the form of speech production, word finding, object naming, grammar, or word comprehension (APA, 2013). Frontotemporal neurocognitive disorder is only diagnosed when Alzheimer's disease has

been ruled out, and the patient must have symptoms that can be characterized as forming a "frontal lobe syndrome" (Rosenstein, 1998). The generic term commonly used to characterize the behaviors associated with this syndrome is executive dysfunction, a concept originally introduced by Luria (1966). Executive function is progressively impaired, and personality changes involving either apathy and indifference or childishness and euphoria occur. Compared with patients with Alzheimer's disease, frontal dementia patients have greater impairment of executive function but relatively better memory and visuoconstructional abilities. The outstanding features all may be viewed as relating to impaired ability to control, regulate, and program behavior. This impairment is manifested in numerous ways, including poor abstraction ability, impaired judgment, apathy, and loss of impulse control. Language is sometimes impaired, but in a rather unique way. Rather than having a formal language disorder, the patient loses the ability to control behavior through language. There is also often a difficulty with narrative speech that has been interpreted as a problem in forming the intention to speak or in formulating a plan for a narrative. Such terms as lack of insight or of the ability to produce goal-oriented behavior are used to describe the frontal lobe patient. In many cases, these activating, regulatory, and programming functions are so impaired that the outcome looks like a generalized dementia with implications for many forms of cognitive, perceptual, and motor activities. Frontal dementia may occur as a result of several processes, such as head trauma, tumor, or stroke, but the syndrome produced is more or less the same.

Major or Mild Neurocognitive Disorder With Lewy Bodies This disorder has a different pathology from Alzheimer's disease, being associated more with Parkinson's disease (Becker, Farbman, Hamilton, & Lopez, 2011; McKeith et al., 2004). The major symptoms are variations in alertness, recurrent hallucinations, and Parkinsonian symptoms (e.g., tremor, rigidity). Lewy bodies are intraneuron inclusion bodies first identified in the substantia nigra of patients with Parkinson's disease.

Major or Mild Vascular Neurocognitive Disorder This is a progressive condition based on a history of small strokes associated with hypertension. Patients with vascular neurocognitive disorder experience a stepwise deterioration of function, with each small stroke making the dementia worse in some way. There are parallels between this disorder and the older concept of cerebral arteriosclerosis in that they both relate to the role of generalized cerebral vascular disease in producing progressive brain dysfunction. However, vascular neurocognitive disorder is actually a much more precisely defined syndrome that, although not rare, is not extremely common, either. Furthermore, although it continues to be a separate diagnosis, there is substantial evidence that vascular neurocognitive disorder overlaps a great deal with Alzheimer's disease. Autopsy studies often show that there is evidence of vascular pathology in individuals diagnosed with Alzheimer's disease, and the reverse is also true. It has been suggested that cardiovascular illness may be a risk factor for Alzheimer's disease. Moreover, there appears to have been an increased focus of interest in the specific vascular disorders, including heart failure, stroke, and arteriovenous malformations, each of which has different cognitive consequences (Festa, 2010; Lantz, Lazar, Levine, & Levine, 2010; Pavol, 2010).

Because this disorder is known to be associated with hypertension and a series of strokes, the end result is substantial deterioration in cognitive functioning. However, the course of the deterioration is not thought to be as uniform as is the case in Alzheimer's disease, but rather is generally described as stepwise and patchy. The patient may remain relatively stable between strokes, and the symptomatology produced may be associated with the site of the strokes. It may be mentioned that whereas these distinctions between vascular and Alzheimer's type dementia are clearly described, in individual patients it is not always possible to make a definitive differential diagnosis. Even such sophisticated radiological methods as the CT scan and MRI do not always contribute to the diagnosis. *DSM-5* recognizes the significance of comorbidity with the statement "Most individuals with Alzheimer's disease are elderly and have multiple medical conditions that can complicate diagnosis and influence the clinical course. Major or mild NCD due to Alzheimer's disease commonly co-occurs with cerebrovascular disease which contributes to the clinical picture" (p. 614).

Major or Mild Neurocognitive Disorder Due to Huntington's Disease The progressive cognitive deterioration seen in Huntington's disease also involves significant impairment of memory, with other abilities becoming gradually affected through the course of the illness. However, it differs from Alzheimer's disease in that it is accompanied by choreic movements and by the fact that the age of onset is substantially earlier than is the case for Alzheimer's disease. Because of the chorea, there is also a difficulty in speech articulation frequently seen, which is not the case for Alzheimer's patients.

There are other major or minor neurocognitive disorders listed in the *DSM-5*, including major or mild neurocognitive disorder due to traumatic brain injury, substance/medication-induced major or mild neurocognitive disorder, major or mild neurocognitive disorder due to HIV infection, major or mild neurocognitive disorder due to prion disease, and major or mild neurocognitive disorder due to Parkinson's disease. Patients diagnosed with these syndromes do not have the specific syndromes of the type described earlier. The deficit pattern tends to be global in nature, with all functions more or less involved, even though some investigators have attempted to identify syndromal subtypes, with some having more deficit in the area of abstraction and judgment, some in the area of memory, and some in regard to affect and personality changes. This typology has recently received support from studies delineating frontotemporal dementia, semantic dementia, and Lewy body dementia as separate entities, but most patients have difficulties with all three areas.

OTHER CONDITIONS IMPORTANT FOR UNDERSTANDING BRAIN FUNCTIONING

In this section we will provide descriptions of the more commonly occurring disorders associated with structural brain damage. It is clear that what is common in one setting may be rare in another. Thus, we will focus on what is common in an adult neuropsychiatric setting. The neuropsychological syndromes found in childhood are often quite different from what is seen in adults and deserve separate treatment. Furthermore, the emphasis will be placed on chronic rather than acute syndromes

because, with relatively rare exceptions, the psychologist and psychiatrist encounter the former type far more frequently than the latter.

THE COMMUNICATIVE DISORDERS

In general, aphasia and related language disorders are associated with unilateral brain damage to the dominant hemisphere, which in most individuals is the left hemisphere. Most aphasias result from stroke, but they can be acquired on the basis of left hemisphere head trauma or from brain tumor. Whereas the definition has changed over the years, the most current one requires the presence of impairment of communicative ability associated with focal, structural brain damage. Thus, the term is not coextensive with all disorders of communicative ability and does not include, for example, the language disorders commonly seen in demented individuals with diffuse brain damage. The study of aphasia has in essence become a separate area of scientific inquiry, having its own literature and several theoretical frameworks. The term *aphasia* does not convey a great deal of clinically significant information, because the various subtypes are quite different from each other.

Numerous attempts have been made to classify the aphasias, and there is no universally accepted system. Contemporary theory indicates that perhaps the most useful major distinction is between fluent and nonfluent aphasias. To many authorities, this distinction is more accurate than the previously more commonly made one between expressive and receptive aphasias. The problem is that people with aphasia with primarily expressive problems do not generally have normal language comprehension, and it is almost always true that people with aphasia with major speech comprehension disturbances do not express themselves normally. However, there are individuals with aphasia who talk fluently and others whose speech is labored, very limited, and halting, if present at all in a meaningful sense. In the case of the former group, while speech is fluent, it is generally more or less incomprehensible because of a tendency to substitute incorrect words for correct ones—a condition known as verbal paraphasia. However, the primary disturbance in these patients involves profoundly impaired auditory comprehension. This combination of impaired comprehension and paraphasia is generally known as Wernicke's aphasia. The responsible lesion is generally in the superior gyrus of the left temporal lobe. In nonfluent aphasia, comprehension is generally somewhat better, but speech is accomplished with great difficulty and is quite limited. This condition is generally known as Broca's aphasia, the responsible lesion being in the lower, posterior portion of the left frontal lobe (i.e., Broca's area). Several other types of aphasia are relatively rare and will not be described here. However, it is important to point out that most aphasias are mixed, having components of the various pure types. Furthermore, the type of aphasia may change in the same patient, particularly during the course of recovery.

The disorders of reading, writing, and calculation may also be divided into subtypes. In the case of reading, our interest here is in the so-called acquired alexias, in which an individual who was formerly able to read has lost that ability because of focal, structural brain damage. The ability to read letters, words, or sentences may be lost. Handwriting disturbances, or agraphia, might involve a disability in writing words from dictation or a basic disability in forming letters. Thus, some agraphic patients can write, but with omissions and distortions relative to what was dictated.

However, some can no longer engage in the purposive movements needed to form letters. Calculation disturbances, or acalculias, are also of several types. The patient may lose the ability to read numbers, to calculate even if the numbers can be read, or to arrange numbers in a proper spatial sequence for calculation. The various syndromes associated with communicative disorders, while sometimes existing in pure forms, often merge together. For example, alexia is frequently associated with Broca's aphasia, and difficulty with handwriting is commonly seen in patients with Wernicke's aphasia. However, there is generally a pattern in which there is a clear primary disorder, such as impaired auditory comprehension, with other disorders, such as difficulty with reading or writing, occurring as associated defects. Sometimes rather unusual combinations occur, as in the case of the syndrome of alexia without agraphia. In this case, the patient can write but cannot read, often to the extent that the patient cannot read what she or he just wrote. Based upon recent research, we would add that academic deficits that are not the product of brain damage acquired during adulthood, nor of inadequate educational opportunity, are frequently seen in adults. Rather, people with these deficits have developmentally based learning disabilities that they never outgrew. The view that learning disability is commonly outgrown has been rejected by most students of this area (Katz, Goldstein, & Beers, 2001).

Disorders of Perception and Motility

The disorders of perception can involve perception of one's body as well as perception of the external world. In the case of the external world, the disorder can involve some class of objects or some geographic location. The disorders of motility to be discussed here will not be primary losses of motor function as in the cases of paralysis or paresis, but losses in the area of the capacity to perform skilled, purposive acts. The set of impairments found in this area is called apraxia. There is also the borderline area in which the neuropsychological defect has to do with the coordination of a sense modality, usually vision, and purposive movement. These disorders are sometimes described as impairment of constructional or visual-spatial relations ability. In some patients the primary difficulty is perceptual, whereas in others it is mainly motoric. The body schema disturbances most commonly seen are of three types. The first has to do with the patient's inability to point to his or her own body parts on command. The syndrome is called autotopognosia, meaning lack of awareness of the surface of one's body. A more localized disorder of this type is finger agnosia, in which, while identification of body parts is otherwise intact, the patient cannot identify the fingers of his or her own hands, or the hands of another person. Finger agnosia has been conceptualized as a partial dissolution of the body schema. The third type of body schema disturbance is right-left disorientation, in which the patient cannot identify body parts in regard to whether they are on the right or left side. For example, when the patient is asked to show the right hand, he or she may become confused or show the left hand. More commonly, however, a more complex command is required to elicit this deficit, such as asking the patient to place the left hand on the right shoulder. The traditional thinking about this disorder is that both finger agnosia and right-left disorientation are part of a syndrome, the responsible brain damage being in the region of the left angular gyrus. However, Benton (1985) has pointed out that the matter is more complicated than that, and the issue of localization involves the

specific nature of these defects in terms of the underlying cognitive and perceptual processes affected.

The perceptual disorders in which the difficulty is in recognition of some class of external objects are called gnostic disorders or agnosias. These disorders may be classified with regard to modality and verbal or nonverbal content. Thus, one form of the disorder might involve visual perception of nonverbal stimuli, and would be called visual agnosia. By definition, an agnosia is present when primary function of the affected modality is intact, but the patient cannot recognize or identify the stimulus. For example, in visual agnosia, the patient can see but cannot recognize what he or she has seen. In order to assure oneself that visual agnosia is present, it should be determined that the patient can recognize and name the object in question when it is placed in his or her hand, so that it can be recognized by touch, or when it produces some characteristic sound, so that it can be recognized by audition. The brain lesions involved in the agnosias are generally in the association areas for the various perceptual modalities. Thus, visual agnosia is generally produced by damage to association areas in the occipital lobes. When language is involved, there is obviously a great deal of overlap between the agnosias and the aphasias. For example, visual-verbal agnosia can really be viewed as a form of alexia. In these cases, it is often important to determine through detailed testing whether the deficit is primarily a disturbance of perceptual recognition or a higher-level conceptual disturbance involving language comprehension. There is a wide variety of gnostic disorders reported in the literature involving such phenomena as the inability to recognize faces, colors, or spoken words. However, they are relatively rare conditions and, when present, they may only persist during the acute phase of the illness. In general, agnosia has been described as "perception without meaning," and it is important to remember that it is quite a different phenomenon from what we usually think of as blindness or deafness.

Sometimes a perceptual disorder does not involve a class of objects but a portion of geographic space. The phenomenon itself is described by many terms, the most frequently used ones being neglect and inattention. It is seen most dramatically in vision, where the patient may neglect the entire right or left side of the visual world. It also occurs in the somatosensory modality, in which case the patient may neglect one side or the other of his or her body. Neglect can occur on either side, but it is more common on the left side, because it is generally associated with right hemisphere brain damage. In testing for neglect, it is often useful to employ the method of double stimulation, for example, in the form of simultaneous finger wiggles in the areas of the right and left visual fields. Typically, the patient may report seeing the wiggle in the right field but not in the left. Similarly, when the patient with neglect is touched lightly on the right and left hand at the same time, he or she may report feeling the touch in only one hand or the other. As in the case of the gnostic disorders, neglect is defined in terms of the assumption of intactness of the primary sensory modalities. Thus, the patient with visual neglect should have otherwise normal vision in the neglected half field, while the patient with tactile neglect should have normal somatosensory function. Clinically, neglect may be a symptom of some acute process and should diminish in severity or disappear as the neuropathological condition stabilizes. For example, visual neglect of the left field is often seen in individuals who have recently sustained right hemisphere strokes, but it can be expected to disappear as the patient recovers.

The apraxias constitute a group of syndromes in which the basic deficit involves impairment of purposive movement occurring in the absence of paralysis, weakness, or unsteadiness. For some time, the distinction has been made among three major types of apraxia: ideomotor, limb-kinetic, and ideational. In ideomotor apraxia, the patient has difficulty in performing a movement to verbal command. In the case of limb-kinetic apraxia, movement is clumsy when performed on command or when the patient is asked to imitate a movement. In ideational apraxia, the difficulty is with organizing the correct motor sequences in response to language. In other words, it may be viewed as a disability in regard to carrying out a series of acts. In addition, there are facial apraxias, in which the patient cannot carry out facial movements to command. These four types are thought to involve different brain regions and different pathways. However, they are all generally conceptualized as a destruction or disconnection of motor engrams or traces that control skilled, purposive movement. Certain of the visual-spatial disorders are referred to as apraxias, such as constructional or dressing apraxia, but they are different in nature from the purer motor apraxias described earlier.

The basic difficulty the patient with a visual-spatial disorder has relates to comprehension of spatial relationships, and in most cases, coordination between visual perception and movement. In extreme cases, the patient may readily become disoriented and lose his or her way when going from one location to another. However, in most cases, the difficulty appears to be at the cognitive level and may be examined by asking the patient to copy figures or solve jigsaw or block design type puzzles. Patients with primarily perceptual difficulties have problems in localizing points in space, judging direction, and maintaining geographic orientation, as tested by asking the patient to describe a route or use a map. Patients with constructional difficulties have problems with copying and block building. So-called dressing apraxia may be seen as a form of constructional disability in which the patient cannot deal effectively with the visual-spatial demands involved in such tasks as buttoning clothing. Whereas visual-spatial disorders can arise from lesions found in most parts of the brain, they are most frequently seen, and seen with the greatest severity, in patients with right hemisphere brain damage. Generally, the area that will most consistently produce the severest deficit is the posterior portion of the right hemisphere. In general, although some patients show a dissociation between visual-spatial and visual-motor or constructional aspects of the syndrome of constructional apraxia, most patients have difficulties on both purely perceptual and constructional tasks.

Amnesia

Whereas some degree of impairment of memory is a part of many brain disorders, there are some conditions in which loss of memory is clearly the most outstanding deficit. When the loss of memory is particularly severe and persistent, and other cognitive and perceptual functions are relatively intact, the patient can be described as having an amnesic syndrome. Dementia patients are often amnesic, but their memory disturbance is embedded in significant generalized impairment of intellectual and communicative abilities. The amnesic patient generally has normal language and may be of average intelligence. As in the case of aphasia and several of the other disorders, there is more than one amnesic syndrome. The differences among them revolve

around what the patient can and cannot remember. The structures in the brain that are particularly important for memory are the limbic system, especially the hippocampus, and certain brainstem structures, including the mammilary bodies and the dorsomedial nucleus of the thalamus.

There are many systems described in the literature for distinguishing among types of amnesia and types of memory. With regard to the amnesias, perhaps the most basic distinction is between anterograde and retrograde amnesia. Anterograde amnesia involves the inability to form new memories from the time of the onset of the illness producing the amnesia, whereas retrograde amnesia refers to the inability to recall events that took place before the onset of the illness. This distinction dovetails with the distinction between recent and remote memory. It is also in some correspondence with the distinction made between short-term and long-term memory in the experimental literature. However, various theories define these terms somewhat differently, and perhaps it is best to use the more purely descriptive terms *recent* and *remote memory* in describing the amnesic disorders. It then can be stated that the most commonly appearing amnesic disorders involve dramatic impairment of recent memory with relative sparing of remote memory. This sparing becomes greater as the events to be remembered become more remote. Thus, most amnesic patients can recall their early lives, but they may totally forget what occurred during the last several hours. This distinction between recent and remote memory possibly aids in explaining why most amnesic patients maintain normal language function and average intelligence. In this respect, an amnesic disorder is not so much an obliteration of the past as it is an inability to learn new material.

Probably the most common type of relatively pure amnesic disorder is alcoholic Korsakoff's syndrome. These patients, while often maintaining average levels in several areas of cognitive function, demonstrate a dense amnesia for recent events with relatively well-preserved remote memory. Alcoholic Korsakoff's syndrome has been conceptualized by Butters and Cermak (1980) as an information-processing defect in which new material is encoded in a highly degraded manner leading to high susceptibility of interference. Butters and Cermak (1980), as well as numerous other investigators, have accomplished detailed experimental studies of alcoholic Korsakoff's patients in which the nature of their perceptual, memory, and learning difficulties has been described in detail. The results of this research aid in explaining numerous clinical phenomena noted in Korsakoff's patients, such as their capacity to perform learned behaviors without recall of when or if those behaviors were previously executed, or their tendency to confabulate or "fill in" for the events of the past day that they do not recall. It may be noted that although confabulation was once thought to be a cardinal symptom of Korsakoff's syndrome, it is only seen in some patients.

Another type of amnesic disorder is seen when there is direct, focal damage to the temporal lobes, and most important, to the hippocampus. These temporal lobe or limbic system amnesias are less common than Korsakoff's syndrome, but they have been well studied because of the light they shed on the neuropathology of memory. These patients share many of the characteristics of Korsakoff's patients but have a much more profound deficit in regard to basic consolidation and storage of new material. When Korsakoff's patients are sufficiently cued and given enough time, they can learn. Indeed, sometimes they can demonstrate normal recognition memory.

However, patients with temporal lobe amnesias may find it almost impossible to learn new material under any circumstances.

In some cases, amnesic disorders are modality specific. If one distinguishes between verbal and nonverbal memory, the translation can be made from the distinction between language and nonverbal abilities associated with the specialized functions of each cerebral hemisphere. It has in fact been reported that patients with unilateral lesions involving the left temporal lobe may have memory deficits for verbal material only, whereas right temporal patients have corresponding deficits for nonverbal material. Thus, the left temporal patient may have difficulty with learning word lists, while the right temporal patient may have difficulty with geometric forms. In summary, whereas there are several amnesic syndromes, they all have in common the symptom of lack of ability to learn new material following the onset of the illness. Sometimes the symptom is modality specific, involving only verbal or nonverbal material, but more often than not it involves both modalities. There are several relatively pure types of amnesia, notably Korsakoff's syndrome, but memory difficulties are cardinal symptoms of many other brain disorders, notably the progressive dementias and certain disorders associated with infection. For example, people with Herpes encephalitis frequently have severely impaired memories, but they have other cognitive deficits as well.

Pseudodementia

Although alterations in brain function can give rise to symptoms that look like functional personality changes, the reverse can also occur. That is, a nonorganic personality change, notably the acquisition of a depression, can produce symptoms that look like they have been produced by alterations in brain function. The term generally applied to this situation is pseudodementia, and it is most frequently seen in elderly people who become depressed. The concept of pseudodementia or depressive pseudodementia is not universally accepted, but it is not uncommon to find elderly patients diagnosed as demented when in fact the symptoms of dementia are actually produced by depression. The point is proven when the symptoms disappear or diminish substantially after the depression has run its course, or the patient is treated with antidepressant medication. Wells (1979, 1980) has pointed out that this differential diagnosis is a difficult one to make, and it cannot be accomplished satisfactorily with the usual examinational, laboratory, and psychometric methods. He suggests that perhaps the most useful diagnostic criteria are clinical features. For example, patients with pseudodementia tend to complain about their cognitive losses, whereas patients with dementia tend not to complain. In a more recent formulation, Caine (1986) pointed to the many complexities of differential diagnosis in the elderly, referring in particular to the abundant evidence for neuropsychological deficits in younger depressed patients, and to the not uncommon coexistence of neurological and psychiatric impairments in the elderly.

In recent years there has been substantial rethinking about the concept of pseudodementia in the direction of characterizing it as a neurobiological disorder associated with demonstrable changes in brain structure. Clinicians have observed that depression may sometimes be the first indicator of Alzheimer's disease, and Nussbaum (1994), based on an extensive review of the literature, concluded that

pseudodementia or late-life depression has a neurological substrate involving subcortical structures and the frontal lobes. He indicated that the probable pathology is leukoaraiosis, diminution in the density of white matter, which particularly involves the subcortex in this disorder. Leukoaraiosis is frequently seen in the MRIs of elderly depressed individuals.

EPIDEMIOLOGY

Returning to the *DSM-5* disorders, the epidemiology of the neurocognitive disorders varies with the underlying disorder, and so is unlike what is the case for most of the other diagnostic categories in the *DSM* system. Here, we will only sample from those disorders in which epidemiological considerations are of particular interest. There are some exceptionally interesting and well-documented findings for multiple sclerosis, in which prevalence is directly related to latitude in which one resides; the farther from the equator, the higher the prevalence (Koch-Henriksen & Sørensen, 2010). Further study of this phenomenon has tended to implicate an environmental rather than an ethnic factor.

The epidemiology of head trauma has been extensively studied, with gender, age, and social class turning out to be important considerations. Head trauma has a higher incidence in males than in females (274 per 100,000 in males and 116 per 100,000 in females in one study; Levin, Benton, & Grossman, 1982). It is related to age, with risk peaking between ages 15 and 24, and occurs more frequently in individuals from lower social classes. Alcohol is a major risk factor, but marital status, preexisting psychiatric disorder, and previous history of head injury have also been implicated. The major causes of head injury are motor vehicle accidents, falls, assaults, and recreational or work activities, with motor vehicle accidents clearly being the major cause (50% to 60%; Smith, Barth, Diamond, & Giuliano, 1998).

The epidemiology of Huntington's disease has also been extensively studied. The disease is transmitted as an autosomal dominant trait, and the marker for the gene has been located on the short arm of chromosome 4 (Gusella et al., 1983). Prevalence estimates vary between 5 and 7 per 100,000. There are no known risk factors for acquiring the disorder, the only consideration being having a parent with the disease. If that is the case, the risk of acquiring the disorder is 50%. A test is now available to detect carriers of the defective gene, and its availability and usage may eventually reduce the prevalence of Huntington's disease.

There is a great interest in the epidemiology of Alzheimer's disease, because the specific cause of the disease is not fully understood, and prevention of exposure to risk factors for Alzheimer's disease and related disorders remains a possibility. General health status considerations do not appear to constitute risk factors, but some time ago there were beliefs that a transmissible infective agent existed, and that exposure to aluminum might be a risk factor. The aluminum hypothesis has largely been discarded. Recently, episodes of head trauma have been implicated as a possible risk factor for Alzheimer's disease (Lye & Shores, 2000). A reasonably solid genetic association involving chromosome 21 trisomy has been formed between what appears to be an inherited form of Alzheimer's disease and Down syndrome.

Much of the epidemiology of the organic mental disorders merges with general considerations regarding health status. Cardiovascular risk factors such as obesity and

hypertension put one at greater-than-usual risk for stroke. Smoking is apparently a direct or indirect risk factor for several disorders that eventuate in brain dysfunction. The association of alcoholism and diagnosis of substance/medication induced major or mild neurocognitive disorder is now relatively widely accepted, although it was controversial at one time. Alcohol most clearly—and, perhaps, several other abused substances—make for significant risk factors.

Until recently, the risk of acquiring brain disease by infection had diminished substantially, but that situation has changed markedly with the appearance of human immunodeficiency virus, or HIV-1 infection, or acquired immunodeficiency syndrome (AIDS) dementia (Bornstein, Nasrallah, Para, & Whitacre, 1993; Grant et al., 1987; Van Gorp, Miller, Satz, & Visscher, 1989; Woods et al., 2009). It has become increasingly clear that AIDS is frequently transmitted to children during pregnancy or in association with breastfeeding. New anti-infection medication is in actual use or in the process of going through extensive clinical trials, and there is great promise of effectiveness.

In summary, the prevalence and incidence of the neurocognitive disorders vary substantially, ranging from very rare to common diseases. The number of risk factors also varies, ranging from complete absence to a substantial number of them. The genetic and degenerative diseases, notably Huntington's and Alzheimer's disease, possess little in the way of risk factors, and there is not much that can be done to prevent their occurrence. The development of a test for risk of transmitting Huntington's disease has opened up the admittedly controversial and complex matter of genetic counseling.

PSYCHOLOGICAL AND BIOLOGICAL ASSESSMENT

In recognition of the complexities involved in relating structural brain damage to behavioral consequences, the field of clinical neuropsychology has emerged as a specialty area within psychology. Clinical neuropsychological research has provided specialized instruments for assessment of brain-damaged patients and a variety of rehabilitation methods aimed at remediation of neuropsychological deficits. This research has also pointed out that brain damage, far from being a single clinical entity, actually represents a wide variety of disorders.

Initially, neuropsychologists were strongly interested in the relationship between localization of the brain damage and behavioral outcome. In recent years, however, it has become evident that localization is only one determinant of outcome, albeit often a very important one. Other considerations include the individual's current age, age when the brain damage was acquired, the premorbid personality and level of achievement, and the pathological process producing the dysfunction. Furthermore, neuropsychologists are now cognizant of the possible influence of various nonorganic factors on their assessment methods, such as educational level, socioeconomic status, and mood states. There has been an increasing interest in sociocultural aspects of neuropsychological assessment, particularly with reference to research and testing in cultures throughout the world that are experiencing significant effects of some brain disease, such as AIDS dementia (Heaton, 2006).

More recently, a third major methodology, neuroradiology is available for the study of neurocognitive disorders. Beyond the earlier development of the computed

tomography (CT) scan, PET and fMRI now allow direct observation of brain function in living individuals while they are engaged in some targeted activity. Using different technologies, these procedures can detect changes when the brain is behaviorally activated. It is now also possible to track conduction from one structure to another while some complex behavior is being performed, such as listening to a word and saying what it is. These methods are known as online procedures because the individual is having recordings made at the same time as the behavior is performed.

A second new development is magnetic resonance spectroscopy (MRS). MRS uses MRI technology, but instead of producing a visualization of brain structure or activity, it generates a chemical profile of the brain. While the individual lies under the magnet, a surface coil placed around the head generates various chemical spectra that provide data about underlying tissue at a microbiological level. In the brain, the phosphorous spectrum produces information about brain metabolism based on the activity of phospholipids that exist in cell membranes. The hydrogen spectrum is most often used to determine the level of a substance called N-acetylaspartate (NAA). NAA level has been found to be associated with integrity of neurons and thus provides an index of neuronal loss, deterioration, or maldevelopment. Therefore, we have a way of examining brain tissue at a molecular biological level in a living individual. PET, fMRI, and MRS have substantially advanced our capability of assessing brain function. Diffusion tensor imaging (DTI) is an MRI-related technique that can evaluate misalignment of axonal white matter as may be found with head injury or some developmental disorders. It evaluates anisotropy associated with diffusion of water mainly in white matter.

In this author's judgment, the major developments over the past years continue to be technological in nature. Increasingly sophisticated techniques have been developed to image the brain, not only structurally as in an X-ray but also functionally. We now have very advanced capacities to image brain activity while the individual is engaging in some form of behavior. At present, functional magnetic resonance imaging (fMRI) is the most widely used of these procedures. It involves performing magnetic resonance imaging while the individual is given tasks to perform and recording changes in brain activity. Thus, for example, it is possible to observe increased activity in the language area of the brain while the person is performing a language task.

New developments have also appeared regarding techniques used to make a pathological diagnosis of Alzheimer's disease in a living person. Previously, the diagnosis could only be made at autopsy. Now there is a neuroimaging procedure that can visualize neurochemical changes in the brain that can make a specific diagnosis. It involves an amyloid-imaging positron emission tomography (PET) tracer called Pittsburgh Compound B that detects amyloid in the brain. Amyloid is known to be central to the pathogenesis of Alzheimer's disease (Fagan et al., 2005; Klunk et al., 2004). There have been advances in the genetics of Alzheimer's disease, with great interest in the apolipoprotein E epsilon 4 allele (APOE4) that appears to be associated with age of onset of the disorder. There has also been substantial interest in mild cognitive impairment (MCI), the mild cognitive deficits that frequently appear in elderly people. The question raised has involved whether occurrence of MCI results in conversion to Alzheimer's disease. Degree of deficits noted on neuropsychological testing has been found to be significantly associated with conversion to Alzheimer's disease, thereby constituting a significant risk factor.

ETIOLOGICAL CONSIDERATIONS

The brain may incur many of the illnesses that afflict other organs and organ systems. It may be damaged by trauma or it may become infected. The brain can become cancerous or can lose adequate oxygen through occlusion of the blood vessels that supply it. The brain can be affected through acute or chronic exposure to toxins, such as carbon monoxide or other poisonous substances. Nutritional deficiencies can alter brain function just as they alter the function of other organs and organ systems. The brain may mature abnormally during pregnancy for various reasons, producing different developmental disorders. Aside from these general systemic and exogenous factors, there are diseases that more or less specifically have the central nervous system as their target. These conditions, generally known as degenerative and demyelinating diseases, include Huntington's disease, multiple sclerosis, Parkinson's disease, and disorders associated with aging.

From the point of view of neuropsychological considerations, it is useful to categorize the various disorders according to temporal and topographical parameters. Thus, certain neuropathological conditions are static and do not change substantially; others are slowly progressive; and some are rapidly progressive. With regard to topography, certain conditions tend to involve focal, localized disease, others multifocal lesions, and still others diffuse brain damage without specific localization. Another very important consideration has to do with morbidity and mortality. Some brain disorders are more or less reversible, some are static and do not produce marked change in the patient over lengthy periods, and some are rapidly or slowly progressive, producing increasing morbidity and eventually leading to death. Thus, some types of brain damage produce a stable condition with minimal changes, some types permit substantial recovery, and other types are in actuality terminal illnesses. It is, therefore, apparent that the kind of brain disorder the patient suffers from is a crucial clinical consideration in that it has major implications for treatment, management, and planning.

Head Trauma

Although the skull affords the brain a great deal of protection, severe blows to the head can produce temporary brain dysfunction or permanent brain injury. The temporary conditions, popularly known as concussions, are generally self-limiting and involve a period of confusion, dizziness, and perhaps double vision. However, there seems to be complete recovery in most cases. In concussion, the brain is not thought to be permanently damaged, but there are exceptions. More serious trauma is generally classified as closed or open head injury. In closed head injury, which is more common, the vault of the skull is not penetrated, but the impact of the blow crashes the brain against the skull and thus may create permanent structural damage. In the case of open head injury, the skull is penetrated by a missile of some kind. Open head injuries occur most commonly during wartime as a result of bullet wounds. They sometimes occur as a result of vehicular or industrial accidents, if some rapidly moving object penetrates the skull. Open head injuries are characterized by the destruction of brain tissue in a localized area. There are generally thought to be more remote effects as well, but usually the most severe symptoms are likely to be

associated with the track of the missile through the brain. Thus, an open head injury involving the left temporal lobe could produce aphasia, whereas similar injury to the back of the head could produce a visual disturbance.

A major neuropsychological difference between open and closed head injury is that although the open injury typically produces specific, localized symptoms, the closed head injury, with the possible exception of subdural hematoma, produces diffuse dysfunction without specific focal symptoms. In both cases, some of these symptoms may disappear with time, whereas others may persist. There is generally a sequence of phases that applies to the course of both closed and open head injury. Often, the patient is initially unconscious and may remain that way for an extremely varying amount of time, ranging from minutes to weeks or months. After consciousness is regained, the patient generally goes through a so-called acute phase, during which there may be confusion and disorientation.

The cognitive residual symptoms of head trauma are extremely varied, because they are associated with whether the injury was open head or closed head and if there was clear tissue destruction. Most often, patients with closed head injury have generalized intellectual deficits involving abstract reasoning ability, memory, and judgment. Sometimes, marked personality changes are noted, often having the characteristic of increased impulsiveness and exaggerated affective responsivity. Patients suffering from the residual of open head injury may have classic neuropsychological syndromes such as aphasia, visual-spatial disorders, and specific types of memory or perceptual disorders. In these cases, the symptoms tend to be strongly associated with the lesion site. For example, a patient with left hemisphere brain damage may have an impaired memory for verbal material such as names of objects, whereas the right hemisphere patient may have an impaired memory for nonverbal material such as pictures or musical compositions. In these cases there is said to be both modality (e.g., memory) and material (e.g., verbal stimuli) specificity. Head trauma is generally thought to be the most frequently seen type of brain damage in adolescents and young adults. It, therefore, generally occurs in a reasonably healthy brain. When the combination of a young person with a healthy brain exists, the prognosis for recovery is generally good if the wound itself is not devastating in terms of its extent or the area of the brain involved. For practical purposes, residual brain damage is a static condition that does not generate progressive changes for the worse. Although there is some research evidence (Walker, Caveness, & Critchley, 1969) that following a long quiescent phase, head-injured individuals may begin to deteriorate more rapidly than normal when they become elderly, and there is some evidence that brain injury may be a risk factor for Alzheimer's disease (Lye & Shores, 2000). However, head-injured individuals may nevertheless have many years of productive functioning. There has been a strong interest in outcome following mild head injury (Levin, Eisenberg, & Benton, 1989), as well as in the specific problems associated with head injury in children (Noggle & Pierson, 2010). It has been frequently pointed out in recent years that trauma is the major cause of death in children, and head trauma among children is not uncommon. Most recently, a marked interest has developed in sports injuries (e.g., Schatz, Pardini, Lovell, Collins, & Podell, 2006), with most studies assessing athletes shortly after sustaining a concussion and evaluating future outcome.

Since the Persian Gulf War era, there has been a substantial increase in the study of head injury, particularly head injuries sustained by veterans, and more specifically by

those who had blast injuries or concussions. Thus far, the results are mixed and the characteristics of persistent postconcussion syndrome and its association with PTSD are far from fully understood. Although standard neuroimaging procedures are typically normal following concussion, studies with DTI show some abnormal findings, as reviewed in Bigler (2008). However, in an individual study by Levin et al. (2010), there were no consequential findings with DTI, with head-injured subjects showing normal functional anisotropy, suggesting the absence of axonal misalignment. Wilk et al. (2010) found no or inconsistent association between self-reported concussion and the presence of persistent postconcussive symptoms. However, Mayer et al. (2010) did report finding white-matter abnormalities based upon DTI studies in patients with mild TBI. The roles of PTSD and depression as mediators of these associations have been stressed (Belanger et al., 2010).

Diseases of the Circulatory System

Current thinking about the significance of vascular disease has changed from the time when it was felt that cerebral arteriosclerosis or "hardening of the arteries" was the major cause of generalized brain dysfunction in the middle-aged and elderly. Although this condition is less common, the status of the heart and the blood vessels are significantly related to the intactness of brain function. Basically, the brain requires oxygen to function, and oxygen is distributed to the brain through the cerebral blood vessels. When these vessels become occluded, circulation is compromised and brain function is correspondingly impaired. This impairment occurs in several ways, perhaps the most serious and abrupt being stroke. A stroke is a sudden total blockage of a cerebral artery caused by blood clot or a hemorrhage. The clot may be a thrombosis formed out of atherosclerotic plaques at branches and curves in the cerebral arteries or an embolism, which is a fragment that has broken away from a thrombus in the heart that has migrated to the brain. Cerebral hemorrhages are generally fatal, but survival from thrombosis or embolism is not at all uncommon. Following a period of stupor or unconsciousness, the most common and apparent postacute symptom is hemiplegia—paralysis of one side of the body. There is also a milder form of stroke known as a transient ischemic attack (TIA), which is basically a temporary, self-reversing stroke that does not produce severe syndromes, or may be essentially asymptomatic. The phrase "silent stroke" or "silent cerebral infarction" is used when stroke-type neuropathology is detected by MRI or related procedures, but there are no apparent symptoms (Das et al., 2008).

Other relatively common cerebrovascular disorders are associated with aneurysms and other vascular malformations in the brain. An aneurysm is an area of weak structure in a blood vessel that may not produce symptoms until it balloons out to the extent that it creates pressure effects or it ruptures. A ruptured aneurysm is an extremely serious medical condition in that it may lead to sudden death. However, surgical intervention in which the aneurysm is ligated is often effective. Arteriovenous malformations are congenitally acquired tangles of blood vessels. They may be asymptomatic for many years, but they can eventually rupture and hemorrhage. They may appear anywhere in the brain, but commonly they occur in the posterior half. The symptoms produced, when they occur, may include headache and neurological signs associated with the particular site.

There are major neuropsychological differences between the individual with a focal vascular lesion, most commonly associated with stroke, and the patient with generalized vascular disease such as vascular dementia. The stroke patient is not only characterized by the hemiplegia or hemiparesis, but sometimes by an area of blindness in the right or left visual fields and commonly by a pattern of behavioral deficits associated with the hemisphere of the brain affected and the locus within that hemisphere. If the stroke involves a blood vessel in the left hemisphere, the patient will be paralyzed or weak on the right side of the body, the area of blindness, if present, will involve the right field of vision, and there will frequently be aphasia. Right hemisphere strokes may produce left-sided weakness or paralysis and left visual field defects but no aphasia. Instead, a variety of phenomena may occur. The patient may acquire a severe difficulty with spatial relations—a condition known as *constructional apraxia*. The ability to recognize faces or to appreciate music may be affected. A phenomenon known as *unilateral neglect* may develop, in which the patient does not attend to stimuli in the left visual field, although it may be demonstrated that basic vision is intact. Sometimes affective changes occur in which the patient denies that he or she is ill and may even develop euphoria.

In contrast with this specific, localized symptom picture seen in the stroke patient, the individual with vascular dementia or other generalized cerebral vascular disease has quite a different set of symptoms. Generally, there is no unilateral paralysis, no visual field deficit, no gross aphasia, and none of the symptoms characteristic of patients with right hemisphere strokes. Rather, there is a picture of generalized intellectual, and to some extent physical, deterioration. If weakness is present, it is likely to affect both sides of the body, and typically there is general diminution of intellectual functions including memory, abstraction ability, problem-solving ability, and speed of thought and action. In the case of the patient with vascular dementia, there may be localizing signs, but there would tend to be several of them, and they would not point to a single lesion in one specific site.

The more common forms of cerebral vascular disease are generally not seen until at least middle age, and for the most part are diseases of the elderly. Clinically significant cerebral vascular disease is often associated with a history of generalized cardiovascular or other systemic diseases, notably hypertension and diabetes. Some genetic or metabolic conditions promote greater production of atheromatous material than is normal, and some people are born with arteriovenous malformations or aneurysms, placing them at higher than usual risk for serious cerebral vascular disease. When a stroke is seen in a young adult, it is usually because of an aneurysm or other vascular malformation. Most authorities agree that stroke is basically caused by atherosclerosis, and so genetic and acquired conditions that promote atherosclerotic changes in blood vessels generate risk of stroke. With modern medical treatment there is a good deal of recovery from stroke with substantial restoration of function. However, in the case of the diffuse disorders, there is really no concept of recovery because they tend to be slowly progressive. The major hope is to minimize the risk of future strokes, through such means as controlling blood pressure and weight.

An area of particular interest is the long-term effects of hypertension on cerebral function, as well as the long-term effects of antihypertensive medication. Reviews written some time ago (Elias & Streeten, 1980; King & Miller, 1990) have demonstrated that hypertension in itself, as well as antihypertensive medication, can impair

cognitive function, but there are no definite conclusions in this area as yet, with studies reporting mixed as well as benign outcomes associated with prudent use of the newer antihypertensive medications (Goldstein, 1986).

Degenerative and Demyelinating Diseases

The degenerative and demyelinating diseases constitute a variety of disorders that have several characteristics in common but that are also widely different from each other in many ways. What they have in common is that they specifically attack the central nervous system, they are slowly progressive and incurable, and although they are not all hereditary diseases, they appear to stem from some often unknown but endogenous defect in physiology. Certain diseases, once thought to be degenerative, have been found not to be so, or are thought not to be so at present. For example, certain dementias have been shown to be caused by so-called slow viruses, whereas multiple sclerosis, the major demyelinating disease, is strongly suspected to have a viral etiology. Thus, in these two examples, the classification would change from degenerative to infectious disease.

The term *degenerative disease* means that, for some unknown reason, the brain or the entire central nervous system gradually wastes away. In some cases, this wasting, or atrophy, resembles what happens to the nervous system in very old people, but substantially earlier than the senile period, perhaps as early as the late forties. The previously made distinction between presenile and senile dementia is not currently used much, apparently based upon the understanding that it is the same disease, most often neurocognitive disorder of the Alzheimer's type, but the research literature continues to be controversial, showing some important neurobiological differences between those who demonstrate presence of the disease before or during late life. Senile dementia is generally diagnosed in elderly individuals when the degree of cognitive deficit is substantially greater than one would expect with normal aging. In other words, not all old people become significantly demented before death. Most of those who do, but who do not have another identifiable disease of the central nervous system, are generally thought to have neurocognitive disorder of the Alzheimer's type, which is thought to account for more cases of cognitive dysfunction than does vascular disease. There is another disorder related to Alzheimer's disease called Pick's disease, but it is difficult to distinguish from Alzheimer's disease in living individuals. The distinction only becomes apparent on autopsy, as the neuropathological changes in the brain are different. Within psychiatry, there is no longer an attempt to differentiate clinically among Alzheimer's, Pick's, and some rarer degenerative diseases. *DSM-5* considers all of these diseases as underlying the disorder known as major or mild neurocognitive disorder due to Alzheimer's disease.

Although much is still not known about the degenerative disorders, much has been discovered in recent years. The major discovery was that Alzheimer's and Huntington's disease (a frequently occurring degenerative disease found in younger adults) are apparently based on neurochemical deficiencies. In the case of Alzheimer's disease, the deficiency is thought to be primarily the group of substances related to choline, one of the neurotransmitters. The disease process itself is characterized by progressive death of the choline neurons—the cells that serve as receptor sites for cholinergic agents, and the presence of a gene that produces amyloid plaques in the

brain. Huntington's disease is more neurochemically complex because three neurotransmitters are involved: choline, GABA, and substance P. The reasons for these neurochemical deficiency states remain unknown, but the states themselves have been described, and treatment efforts have been initiated based on this information. For example, some Alzheimer's patients have been given choline or lecithin, a substance related to choline, and other newer drugs such as Aricept, in the hope of slowing down the progression of the illness.

Most recently, an extensive literature has developed around progressive dementias that resemble but are pathologically or behaviorally different from Alzheimer's disease. One group is now known as prion diseases. Prions are proteins that are infectious and can transmit biological information. They also are apparently associated with Creutzfeldt-Jakob disease, a progressive dementia.

ALCOHOLISM

The term *alcoholism* in the context of central nervous system function involves not only the matter of excessive consumption of alcoholic beverages, but also a complex set of considerations involving nutritional status, related disorders such as head trauma, physiological alterations associated with the combination of excessive alcohol consumption and malnutrition, and possible genetic factors. What is frequently observed in long-term chronic alcoholism is a pattern of deterioration of intellectual function not unlike what is seen in patients with major or minor neurocognitive disorders of the Alzheimer's type. However, it is not clear that the deteriorative process is specifically associated with alcohol consumption per se. Thus, although some clinicians use the term *alcoholic dementia*, this characterization lacks sufficient specificity, because it is rarely at all clear that the observed dementia is in fact solely a product of excessive use of alcohol. Looking at the matter in temporal perspective, there first of all may be a genetic propensity for the acquisition of alcoholism that might ultimately have implications for central nervous system function (Goodwin, 1979). Second, Tarter (1976) has suggested that there may be an association between having minimal brain damage or a hyperactivity syndrome as a child and the acquisition of alcoholism as an adult. These two considerations suggest the possibility that at least some individuals who eventually become alcoholics may not have completely normal brain function anteceding the development of alcoholism. Third, during the course of becoming chronically alcoholic, dietary habits tend to become poor, and multiple head injuries may be sustained as a result of fights or accidents. As the combination of excessive alcohol abuse and poor nutrition progresses, major physiological changes may occur, particularly in the liver, and to some extent in the pancreas and gastrointestinal system. Thus, the dementia seen in long-term patients with alcoholism may well involve a combination of all of these factors in addition to the always-present possibility of other neurological complications.

The majority of alcoholics who develop central nervous system complications manifest it in the form of general deterioration of intellectual abilities, but some develop specific syndromes. The most common of these is the Wernicke-Korsakoff syndrome, which begins with the patient going into a confusional state, accompanied by difficulty in walking and controlling eye movements, and by polyneuritis, a condition marked by pain or loss of sensation in the arms and legs. The latter

symptoms may gradually disappear, but the confusional state may evolve into a permanent, severe amnesia. When this transition has taken place, the patient is generally described as having Korsakoff's syndrome or alcohol amnestic disorder, and is treated with large dosages of thiamine, because the etiology of the disorder appears to be a thiamine deficiency rather than a direct consequence of alcohol ingestion. Data reported previously (Blass & Gibson, 1977) indicate that the thiamine deficiency must be accompanied by an inborn metabolic defect related to an enzyme that metabolizes thiamine and is associated with thiamine transport genes (Guerrini, Thomson, & Gurling, 2009). It should be noted that the amnesic and intellectual disorders found in chronic alcoholics are permanent and present even when the patient is not intoxicated. The acute effects of intoxication or withdrawal (e.g., delirium tremens [DTs]) are superimposed on these permanent conditions. These disorders are also progressive as long as the abuse of alcohol and malnutrition persist. Other than abstinence and improved nutrition, there is no specific treatment. Even thiamine treatment for the Korsakoff patient does not restore memory; it is used primarily to prevent additional brain damage.

It is probably fair to say that a major interest in recent years has been the genetics of alcoholism. There is a growing, probably well-justified, belief that a positive family history of alcoholism puts an individual at increased risk for becoming alcoholic, if exposed to alcoholic beverages. The body of supporting research done is broad-ranging, including extensive family adoption studies (Goodwin, Schulsinger, Hermansen, Guze, & Winokur, 1973); neuropsychological studies of relatives (Schaeffer, Parsons, & Yohman, 1984) and children of alcoholics (Tarter, Hegedus, Goldstein, Shelly, & Alterman, 1984); psychophysiological studies, emphasizing brain event–related potentials in siblings (Steinhauer, Hill, & Zubin, 1987) and of children of alcoholics (Begleiter, Porjesz, Bihari, & Kissin, 1984) and laboratory genetic studies. In summary, an extensive effort is being made to find biological markers of alcoholism (Hill, Steinhauer, & Zubin, 1987) and to determine the transmission of alcoholism in families. At this time, several susceptibility genes have been identified (Hill et al., 2004). One reasonable assumption is that alcoholism is a heterogeneous disorder, and there may be both hereditary and nonhereditary forms of it (Cloninger, Bohman, & Sigvardsson, 1981).

Toxic, Infectious, and Metabolic Illnesses

Exogenous or endogenous agents may poison the brain or it may become infected. Sometimes these events occur with such severity that the person dies, but more often, the individual survives with a greater or lesser degree of neurological dysfunction. Beginning with the exogenous toxins, we have already discussed the major one: alcohol. However, excessive use of drugs such as bromides and barbiturates may produce at least temporary brain dysfunction, such as delirium.

In psychiatric settings, a fairly frequently seen type of toxic disorder is carbon monoxide poisoning. This disorder and its treatment are quite complex, because it usually occurs in an individual with a major mood or psychotic disorder who attempted to commit suicide by inhaling car fumes in a closed garage. The brain damage sustained during the episode may often be permanent, resulting in significant intellectual and physical dysfunction in addition to the previously existing psychiatric disorder. Other toxic substances that may affect central nervous system function

include certain sedative and hypnotic drugs, plant poisons, heavy metals, and toxins produced by certain bacteria, leading to such conditions as tetanus and botulism. The specific effects of these substances themselves, as well as of whether exposure is acute (as in the case of tetanus or arsenic poisoning) or chronic (as in the case of addiction to opiates and related drugs), are often crucial.

Many brain disorders are associated with inborn errors of metabolism. In some way a fault in metabolism produces a detrimental effect on the nervous system, generally beginning in early life. There are so many of these disorders that we will only mention two of the more well-known ones as illustrations. The first is phenylketonuria (PKU). PKU is an amino acid uria, a disorder that involves excessive excretion of an amino acid into the urine. It is genetic and, if untreated, can produce intellectual disability accompanied by poor psychomotor development and hyperactivity. The treatment involves a diet low in a substance called phenylalanine. The second disorder is Tay-Sachs disease. The enzyme abnormality here is a deficiency in a substance called hexasaminidase A, which is important for the metabolism of protein and polysaccharides. It is hereditary, occurs mainly in Jewish children, and is present from birth. The symptoms are initially poor motor development and progressive loss of vision, followed by dementia, with death usually occurring before age 5. These two examples illustrate similarity in process, which is basically an inherited enzyme deficiency, but variability in outcome. PKU is treatable, with a relatively favorable prognosis, whereas Tay-Sachs is a rapidly progressive, incurable terminal illness.

Bacterial infections of the brain are generally associated with epidemics but sometimes are seen when there are no epidemics at large. They are generally referred to as encephalitis, when the brain is infected, or meningitis, when the infection is in the membranous tissue that lines the brain, known as the meninges. Infections, of course, are produced by microorganisms that invade tissue and produce inflammation. During the acute phase of the bacterial infections, the patient may be quite ill, and survival is an important issue. Headaches, fever, and a stiff neck are major symptoms. There may be delirium, confusion, and alterations in state of consciousness ranging from drowsiness, through excessive sleeping, to coma. Some forms of encephalitis were popularly known as "sleeping sickness." Following the acute phase of bacterial infection, the patient may be left with residual neurological and neuropsychological disabilities and personality changes. Sometimes infections are local, and the patient is left with neurological deficits that correspond with the lesion site. The irritability, restlessness, and aggressiveness of postencephalitic children are mentioned in the literature. Jervis (1959) described them as overactive, restless, impulsive, assaultive, and wantonly destructive.

Neurosyphylis is another type of infection that has a relatively unique course. Most interesting, aside from the progressive dementia that characterizes this disorder, are the major personality changes involving the acquisition of delusions and a tendency toward uncritical self-aggrandizement. Although neurosyphilis or general paresis played a major role in the development of psychiatry, it is now a relatively rare disease and is seldom seen in clinical practice. Similarly, the related neurosyphilitic symptoms, such as tabes dorsalis and syphilitic deafness, are also rarely seen.

The incidence and perhaps the interest in the bacterial infections and neurosyphilis have diminished, but interest in viral infections has increased substantially during recent years. There are perhaps four reasons for this phenomenon: (1) Jonas Salk's

discovery that poliomyelitis was caused by a virus and could be prevented by vaccination; (2) the recent increase in the incidence of herpes simplex, which is a viral disorder; (3) the appearance of AIDS; and (4) the discovery of the "slow viruses." The latter two reasons are probably of greatest interest in the present context. With regard to the slow viruses, it has been discovered that certain viruses have a long incubation period and may cause chronic degenerative disease, resembling Alzheimer's disease in many ways. Thus, some neurocognitive disorders may be produced by a transmittable agent. One of these disorders appears to be a disease known as kuru, and another is known as Creutzfeldt-Jakob disease. Recently, there has been an outbreak of a related disorder called mad cow disease, or bovine spongiform encephalopathy (Balter, 2001). The importance of the finding is that the discovery of infection as the cause of disease opens the possibility of the development of preventive treatment in the form of a vaccine.

Major and mild neurocognitive disorder due to AIDS is another form of viral encephalopathy. It is a consequence of human immunovirus (HIV) infection and apparently represents an illness that has not appeared on the planet previously. It has been characterized as a progressive subcortical dementia of the type seen in patients with Huntington's disease and other neurological disorders in which the major neuropathology is in the subcortex. The syndrome has not been completely described, but there is substantial evidence of neuropsychological abnormalities. The first papers in this area appeared circa 1987, with the best-known study being that of Grant et al. (1987). A review is contained in Bornstein et al. (1993), and recent updates have been provided by Heaton (2006) and Woods et al. (2009).

ETIOLOGICAL CONSIDERATIONS

The neurocognitive disorders are based on some diseases of known genetic origin, some diseases in which a genetic or familial component is suspected, and some that are clearly acquired disorders. It is well established that Huntington's disease and certain forms of intellectual disability, notably Down syndrome, are genetic disorders. There appears to be evidence that there is a hereditary form of Alzheimer's disease, although the genetic contribution to Alzheimer's disease in general is not fully understood. A relatively rare genetic subtype has been identified consisting of patients who develop psychosis (DeMichele-Sweet & Sweet, 2010). The great majority of individuals with this subtype and other individuals with Alzheimer's disease have a gene on chromosome 14 called Apolipoprotein E that promotes development of the amyloid plaques that constitute the major brain pathology associated with the disease. Whether multiple sclerosis has a genetic component remains under investigation, although it is clearly not a hereditary disorder like Huntington's disease.

Of great recent interest is the role of genetics in the acquisition of alcoholism, and subsequently dementia associated with alcoholism or alcohol amnestic disorder. Evidence suggests that having an alcoholic parent places one at higher than average risk for developing alcoholism. The specific genetic factors are far from understood, but the association in families appears to be present. Whether having a family history of alcoholism increases the risk of acquiring dementia associated with alcoholism is not clear, but it has been shown that nonalcoholic sons of alcoholic fathers do more poorly on some cognitive tests than do matched controls. The matter is substantially

clearer in the case of alcohol amnestic disorder or Korsakoff's syndrome. A widely cited study by Blass and Gibson (1977) showed acquisition of Korsakoff's syndrome is dependent upon the existence of a genetic defect in a liver enzyme called transketolase in combination with a thiamine deficiency.

Other genetic and familial factors associated with the organic mental disorders relate largely to the genetics of underlying systemic disorders. Thus, the genetics of cancer might have some bearing on the likelihood of acquiring a brain tumor, while the genetics of the cardiovascular system might have some bearing on the risk for stroke. Disorders such as hypertension and diabetes appear to run in families and have varying incidences in different ethnic groups. Ethnic specificity is sometimes quite precise (but this is rare), as in the case of Tay-Sachs disease, a degenerative disorder of early childhood that is found almost exclusively in Eastern European Jews.

COURSE AND PROGNOSIS

Course and prognosis for the neurocognitive disorders also vary with the underlying disorder. We will review the basic considerations here by first introducing some stages of acceleration and development. Then we will provide examples of disorders that have courses and prognoses consistent with various acceleration and developmental combinations. The acceleration stages are steady state, slow, moderate, and rapid. The developmental stages are the perinatal period, early childhood, late childhood and adolescence, early adulthood, middle age, and old age. The acceleration stages have to do with the rate of progression of the disorder, whereas the developmental stages characterize the age of onset of symptoms.

Intellectual disability would be a disorder with a course involving onset during the perinatal period and steady-state acceleration. Intellectual disability is one of those disorders in which there is little if any progression of neuropathology, but there may be a slowly progressive disability because of increasing environmental demands for cognitive abilities that the individual does not possess. Other developmental disorders, such as specific learning disability, do not have their onsets during the perinatal period but rather during early childhood when academic skills are first expected to be acquired.

In contrast to these disorders, stroke is typically characterized by onset during middle age. The acceleration of the disorder is first extremely rapid and then slows down, gradually reaching steady state. Thus, the stroke patient, at the time of the stroke, becomes seriously ill very rapidly, and this is followed by additional destructive processes in the brain. Assuming a good outcome, a gradual recovery period follows, and there is restoration of the brain to a relatively normal steady state. On the other hand, malignant brain tumors, which also tend to appear during middle age, progress rapidly and do not decelerate unless they are successfully surgically removed.

The progressive dementias generally appear during middle or old age and accelerate slowly or moderately. Huntington's disease generally progresses less rapidly than Alzheimer's disease, and so the Huntington's patient may live a long life with his or her symptoms. Head trauma is a disorder that may occur at any age, but once the acute phase of the disorder is over, the brain typically returns to a steady state. Thus, the head-trauma patient, if recovery from the acute condition is

satisfactory, may have a normal life expectancy with an often-dramatic picture of deterioration immediately following the trauma until completion of resolution of the acute phase followed by substantial recovery. However, the degree of residual disabilities may vary widely.

Briefly summarizing these considerations from a developmental standpoint, the most common organic mental disorder associated with the perinatal period is intellectual disability and its variants. During early childhood, the specific and pervasive developmental disorders begin to appear. Head trauma typically begins to appear during late childhood and adolescence, and incidence peaks during young adulthood. Systemic illnesses, notably cardiovascular, cardiopulmonary, and neoplastic disease, most commonly impact negatively on brain functions during middle age. Dementia associated with alcoholism also begins to appear during early middle age. The progressive degenerative dementias are largely associated with old age.

With regard to acceleration, following the time period surrounding the acquisition of the disorder, developmental, vascular, and traumatic disorders tend to be relatively stable. Malignant tumors and certain infectious disorders may be rapidly progressive, and the degenerative disorders progress at a slow to moderate pace. Although the connotation of the term *progressive* is progressively worse, not all the neurocognitive disorders remain stable or get worse. There is recovery of certain disorders as a natural process or with the aid of treatment. In the case of head trauma, there is a rather typical history of initial unconsciousness, lapsing into coma for a varying length of time, awakening, a period of memory loss and incomplete orientation called posttraumatic amnesia, and resolution of the amnesia. Rehabilitation is often initiated at some point in this progression, sometimes beginning while the patient is still in a coma. The outcome of this combination of spontaneous recovery and rehabilitation is rarely, if ever, complete return to preinjury status, but often allows for a return to productive living in the community. Recovery from stroke is also common, and many poststroke patients can return to community living. Among the most important prognostic indicators for head trauma are length of time in coma and length of posttraumatic amnesia. General health status is a good predictor for stroke outcome and potential for recurrence. Patients who maintain poor cardiac status, hypertension, inappropriate dietary habits, or substance abuse are poorer candidates for recovery than are poststroke patients who do not have these difficulties. Some patients, particularly those with chronic, severe hypertension, may have multiple strokes, resolving into a vascular dementia.

There is increasing evidence that rehabilitation of head trauma may often have beneficial effects over and above spontaneous recovery. With regard to the developmental disorders, enormous efforts have been made in institutional and school settings to provide appropriate educational remediation for developmentally disabled children, often with some success. Effective treatment at the time of onset of acute disorder also has obvious implications for prognosis. Use of appropriate medications and management following trauma or stroke, and the feasibility and availability of neurosurgery, are major considerations. Tumors can be removed, aneurysms can be repaired, and increased pressure can be relieved by neurosurgeons. These interventions during the acute phase of a disorder are often mainly directed toward preservation of life, but they also have important implications for the outcomes of surviving patients.

SUMMARY

The diagnostic category of Neurocognitive Disorders, formerly known as delirium, dementia, and amnestic and other cognitive disorders—and as organic mental disorders before that—consists of many conditions in which behavioral changes may be directly associated with some basis in altered brain function. Although the general diagnostic term *organic brain syndrome* has commonly been used to describe these conditions, the wide variability in the manifestations of brain dysfunction makes this term insufficiently precise in reference to clinical relevance, and it has been abandoned. It was pointed out that the variability is attributable to several factors, including the following considerations: (a) the location of the damage in the brain, (b) the neuropathological process producing the damage, (c) the length of time the brain damage has been present, (d) the age and health status of the individual at the time the damage is sustained, and (e) the individual's premorbid personality and level of function.

The neuropsychological approach to the conceptualization of these disorders has identified behavioral parameters along which the manifestations of brain dysfunction can be described and classified. The most frequently considered dimensions are intellectual function, language, attention, memory, visual spatial skills, perceptual skills, and motor function. Some important concepts related to brain function and brain disorders include the principle of contralateral control of perceptual and motor functions and functional hemisphere asymmetries. In addition, studies of brain-damaged patients have shown that particular structures in the brain mediate relatively discrete behaviors. Neurologists and neuropsychologists have identified several syndromes in such areas as language dysfunction, memory disorder, and general intellectual impairment. It was pointed out that there are also major variations in the courses of neurocognitive disorders. Some are transient, leaving little or no residua; some are permanent but not progressive; others are either slowly or rapidly progressive. Whereas these disorders most profoundly and commonly involve impairment of cognitive, perceptual, and motor skills, sometimes personality changes of various types are the most prominent symptoms. More often than not, personality and affective changes appear in brain-damaged patients along with their cognitive, perceptual, and motor disorders. Thus, a mood disorder or such symptoms as delusions and hallucinations may be sequelae of brain damage for various reasons.

During the years spanning the writing of the various editions of this chapter, there have been several major developments in the area of what was originally called the organic mental disorders. There has been the appearance of at least one new disorder, AIDS dementia, major discoveries in the genetics of Huntington's disease and alcoholism, enormous developments in the technology of neuroimaging, growth of a field of neurotoxicology producing knowledge about the epidemiology of neurodevelopmental disorders in particular, and a reconceptualization by psychiatry of the previously held distinction between functional and organic disorders. The work in neuroimaging is particularly exciting, because it goes beyond obtaining more refined pictures of the brain and now allows us to observe the working of the brain during ongoing behavior through fMRI, and to examine the molecular biology of brain function through MRS.

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CHAPTER 20

Personality Disorders

CHRISTOPHER J. HOPWOOD and KATHERINE M. THOMAS

PERSONALITY DISORDERS (PDs) represent a major public health concern, as more than 1 in 10 adults in the community meet the diagnostic criteria for at least one PD (Torgersen, 2005; Torgersen, Kringlen, & Cramer, 2001) and PD diagnoses are associated with increased risk for hospitalization (Bender et al., 2001), criminal behavior (Johnson et al., 2000), suicidal behavior (Soloff, Lis, Kelly, & Cornelius, 1994), and dysfunction at work and in relationships (Grant et al., 2004; Skodol et al., 2002; Torgersen, 2005). Relatively few evidence-based treatments are available for PDs (Matusiewicz, Hopwood, Banducci, & Lejuez, 2010), which are notoriously difficult to treat and interfere with treatment of other kinds of disorders (Cyranowski et al., 2004; Feske et al., 2004; Reich, 2003). The wide-ranging clinical importance of normative personality traits thought to predispose personality and other forms of psychopathology is also well-documented (e.g., Lahey, 2009; Ozer & Benet-Martinez, 2006; Roberts, Kuncel, Shiner, Caspi, & Goldberg, 2007). For instance, Cuijpers et al. (2010) estimated that the direct and indirect medical costs for individuals in the top 5% of neuroticism scores are $12,362 per person per year, compared with $7,851 for individuals with mood disorders and $3,641 for the average person.

Despite the clinical significance of personality and personality pathology, representing PDs in a manner that is scientifically valid and clinically useful continues to pose a major challenge. In the run-up to the publication of *DSM-5*, the view that the *DSM-III* and *DSM-IV* model of PDs that has guided recent research and practice is substantially flawed has been commonly advanced, and many alternatives have been suggested (Bornstein, 1997; Clark, 2007; Hopwood et al., 2011; Krueger, Eaton, Derringer, et al., 2011; Westen, Shedler, & Bradley, 2006; Widiger & Mullins-Sweat, 2009). Although it seemed that changes to the PDs in the *DSM-5* would be dramatic (Bender, Morey, & Skodol, 2011; Krueger, Eaton, Clark, et al., 2011; Skodol et al., 2011), in the end the Board of Trustees of the American Psychiatric Association voted to retain the *DSM-IV* system in *DSM-5*. However, they also included an alternative formulation in *DSM-5*, Section III. The new framework has the potential to increase clinical utility and efficiency, more closely link the PDs with evidence-based models of personality and personality pathology, and ultimately lead to an increased focus on personality and PD among clinicians and scholars, with a corresponding improvement in practice and research. However, the proposed

DSM-5 model is not without critics, who have expressed concerns both about its clinical utility (Bornstein, 2011b; Clarkin & Huprich, 2011; Shedler et al., 2010) and its evidentiary basis (Samuel, 2011; Widiger, 2011; Zimmerman, 2011). Addressing these concerns is the next major step in PD research, as this will facilitate the migration of an improved system, like the one in Section III, into the official diagnostic nomenclature. Nevertheless, given that *DSM-5* PDs are essentially *DSM-IV* PDs, in this chapter we focus on the *DSM-IV* model.

We begin this chapter by discussing several concepts relevant to the definition of personality pathology and PD. We next describe the *DSM-IV* PDs in a historical context, review research on the prevalence, etiology, and course of personality pathology, and describe several approaches to its assessment. We close with a review of the *DSM-5* proposal, highlighting differences between the *DSM-IV* and *DSM-5* approaches to PD diagnosis in the context of a clinical case.

DEFINING PERSONALITY: TRAITS, DYNAMICS, PATHOLOGY, AND DISORDERS

Personality is a broad concept with considerable room for theoretical variation in terms of emphasis on different, even nonoverlapping, components. One way to organize divergent theoretical perspectives is to differentiate those aspects of personality on which they focus. For instance, a protracted rivalry exists in academic personality psychology between those who focus on its more stable or dynamic aspects that extend to the problem of how to classify personality pathology (Wright, 2011). There are also vigorous debates between those who would prefer a more conservative approach to diagnosis involving the retention of categorical PD constructs (e.g., Bornstein, 2011a; Gunderson, 2010; Shedler et al., 2010) and those who would overhaul the model more dramatically by utilizing a completely dimensional approach (e.g., Widiger & Mullins-Sweat, 2009; Krueger et al., 2011).

The *DSM-III* and *DSM-IV* circumvented conceptual debates somewhat by focusing on atheoretical descriptions of personality pathology. The *DSM-IV* defines PD as "an enduring pattern of inner experience and behavior that deviates markedly from the expectations of the individual's culture, is pervasive and inflexible, has an onset in adolescence or early adulthood, is stable over time, and leads to distress or impairment" (APA, 2000, p. 685). The *DSM-IV* describes 10 instantiations of PD, organized into three clusters: Cluster A: schizotypal, schizoid, and paranoid; Cluster B: antisocial, borderline, histrionic, and narcissistic; and Cluster C: avoidant, dependent, and obsessive-compulsive.

These specific PDs, their clustering, and their criteria were selected as much based on clinical legacy in the medical and psychoanalytic perspectives on personality and the collective wisdom of a specific group of committee members with diverse theoretical perspectives, as they were for their empirical support or conceptual coherence (Widiger, 1993). While the atheoretical approach of the *DSM-III* and *DSM-IV* had many advantages, notably its apparently having affected a dramatic increase in PD research, it has become clear that important conceptual issues must be addressed more directly for PD classification to move forward. To clarify some of these conceptual issues, we begin by distinguishing four broad domains of personality that are relevant to debates on the nature of personality and related pathology: traits,

dynamics, pathology, and disorders. These definitions provide a framework for discussing various perspectives on PD classification in the remainder of this chapter.

Personality Traits

Personality traits are enduring features of personality that are (a) cultural universal (McCrae & Terracciano, 2005); (b) heritable (Jang, Livesley, & Vernon, 1996); (c) linked to specific neurobiological structures (DeYoung, 2010) and pathways (Depue & Lenzenweger, 2005); (d) well-characterized in terms of content and course (Soldz & Valliant, 2002); (e) valid for predicting a host of important life outcomes (Roberts et al., 2007); and (f) amenable to reliable assessment, particularly via self-report questionnaires (Samuel & Widiger, 2006). The Five-Factor Model (FFM) currently represents the most viable model of normative personality traits, having the advantage of decades of empirical justification (Digman, 1990) and extensive theoretical articulation (Costa & McCrae, 2006). In the FFM, five normally distributed traits represent the broadest level of variation in personality: neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness. These traits provide a context for all human behavior, and certain constellations of these traits make personality pathology in general and certain forms of PD more or less likely (Morey et al., 2002; Samuel & Widiger, 2008; Saulsman & Page, 2004).

From the perspective of the *DSM-IV*, personality traits such as those of the FFM are enduring features with broad implications for behavior across many situations. These features become clinically relevant when they are "inflexible and maladaptive and cause significant functional impairment or subjective distress" (APA, 2000, p. 686). This distinction implies a discontinuity between traits and their maladaptive consequences under conditions of inflexibility and extremity. However, an explicit linkage between traits and associated dysfunction invites a dimensional view of personality pathology, in which differences between trait and PD are quantitative rather than qualitative. Indeed, evidence suggests that the cluster model of the *DSM-IV* is not valid (Lenzenweger & Clarkin, 2005) and that the disorders are overlapping blends of polythetic and potentially common traits (Widiger et al., 1991), suggesting scientific advantages to viewing personality pathology dimensionally. These potential advantages have led some theorists to suggest defining PDs as reflecting extreme or maladaptive variants of normative traits (Widiger, 1993).

However, several research findings prescribe pause in equating personality pathology with extreme scores on normative traits (Hopwood, 2011). First, relations between normative traits and PDs are not unique or special; normative traits relate systematically to most forms of psychopathology (Cuijpers et al., 2010; Kotov, Gomez, Schmidt, & Watson, 2010), just as they relate to a wide variety of individual differences in human behavior (Ozer & Benet-Martinez, 2006). Second, there are potential structural differences between normal and pathological personality traits (Krueger, Eaton, Derringer, et al., 2011). Third, personality traits and disorders can be distinguished empirically in terms of stability and incremental validity (Hopwood & Zanarini, 2010; Morey et al., 2012; Morey & Hopwood, 2013; Morey & Zanarini, 2000). Stable trait concepts are also limited for conceptualizing dynamic and contingent aspects of social behavior and emotional experiences related to personality and related pathology, which we describe next.

Personality Dynamics

Mischel's 1968 text *Personality and Assessment* initiated a major conflict in personality psychology between those who view personality as made up of stable traits and those who see personality primarily as a function of situational contingencies (see *Journal of Research in Personality, 43*[2]). Although it has been difficult and contentious, this debate has had several positive consequences. With regard to personality stability, trait psychologists were prompted to develop methods that could more convincingly show that traits can be reliably assessed, are stable, and are valid predictors of important behaviors. Equally relevant to contemporary models of PD, this debate led to the development of new models for understanding how traits and situations interact in *if . . . then* behavioral signatures (Mischel & Shoda, 1995). For instance, *if* a conscientious person is on the clock, *then* she will typically attend to her work. This logic extends to PD (Wright, 2011): *If* a person with borderline PD is exposed to rejection, *then* he will tend to react in a self-damaging manner. Notably, this formulation, while inconsistent with a simple trait-behavior formulation of personality (Clarkin & Huprich, 2011), is consonant with several previous models, including Lewin's (1936) classic equation that personality is a function of the person and the environment, or object-relations models that assert that behavior is influenced by the elicitation of self-other dyad units by the parameters of current, actual social situations (Kernberg & Caligor, 2005). As such, the concept of the behavioral signature both reemphasizes and builds upon a long tradition in personality and clinical psychology that emphasizes the moderation of trait-relevant behavior by situational contingencies.

Understanding dynamic elements of personality may be particularly important given recent research suggesting that PD symptoms vary in their stabilities (McGlashan et al., 2005). However, research aimed at conceptualizing the behavioral signatures associated with PDs is just beginning. Most of the work in this area has involved borderline PD, likely because intraindividual variability in emotion and behavior is thematic of the disorder (Schmideberg, 1959). Research using ecological momentary assessment—in which assessments occur several times per day over several days—has generally showed increased variability in mood, interpersonal behavior, and self-esteem among borderline individuals (Sadikaj, Russell, Moskowitz, & Paris, 2010; Trull et al., 2008; Zeigler-Hill & Abraham, 2006). Ongoing and future work exploring the intraindividual dynamics associated with particular kinds of personality problems will be important for assimilating dynamic behavioral signatures into conceptualizations of personality pathology and PD.

Severity of Personality Pathology

Several PD theorists have distinguished defining features of personality pathology from the stylistic manifestations of personality disorders (Bornstein, 2011a; Kernberg, 1984; Livesley, 1998; Pincus, 2005; Pincus & Hopwood, 2012). From this perspective, personality pathology indicates whether a person has a clinically significant PD diagnosis as well as the overall level or severity of personality-related dysfunction, whereas PDs (described later) reflect symptom constellations that vary across individuals, independent of the severity of their overall personality pathology. For

example, the *DSM-IV* distinguishes the defining characteristics of PD in general from symptom criteria for 10 specific PD types. However, in the *DSM-IV* model, personality pathology is not quantified, and the PD symptoms conflate aspects of pathological severity and its stylistic manifestations. This conflation likely contributes to unnecessarily high comorbidity among the PDs (Parker et al., 1998).

Research supports the distinction between personality pathology and stylistic aspects of PDs. Parker et al. (2004) derived two higher-order factors from an assessment of the basic elements of personality pathology, which they labeled cooperativeness (ability to love) and coping (ability to work). These factors correlated nonspecifically with PDs and differentiated clinical and nonclinical samples. Hopwood et al. (2011) factor-analyzed PD symptoms after variance in each symptom associated with a general pathology factor was removed. The severity composite explained most of the variance in functional outcomes, but the five stylistic dimensions, which were labeled peculiarity, deliberateness, instability, withdrawal, and fearfulness, incremented this composite for predicting several specific outcomes. Importantly, these stylistic dimensions were completely independent of the overall level of personality pathology severity and were mostly independent of normative traits. Morey et al. (2011) assessed personality pathology with items from questionnaires designed to assess global personality dysfunction. By refining these item sets using a host of psychometric procedures, they showed, in two large and diverse samples, that greater severity was associated with greater likelihood of PD diagnosis and higher rates of comorbidity.

Personality Disorder Style

Delineating stylistic aspects of PD would represent a significant challenge even if global personality pathology were effectively separated from PD features. The *DSM-IV* proposes 10 PDs, but given the conflation of severity and style in the *DSM-IV* (Parker et al., 1998), it is possible that fewer than 10 stylistic dimensions would be sufficient for depicting the stylistic variability in PD expression. The Hopwood et al. (2011) study discussed previously identified five reliable PD dimensions, although that study was constrained by the *DSM-IV* content that was factor-analyzed. To the degree that the *DSM-IV* symptom criteria are not comprehensive (e.g., they do not include symptoms from appendicized diagnoses and may not fully capture the content of some disorders [e.g., Pincus, Wright, Hopwood, & Krueger, 2011]), it is possible that other important dimensions exist. Thus, an important question for ongoing research is: How many PD dimensions are there?

We will discuss this issue in more detail, but for now we suggest that decisions about what PDs to keep or remove and whether PDs should be conceptualized as polythetic syndromes or trait constellations should be based on quantitative evidence. Given that evidence is currently insufficient for such decisions, contemporary decisions about how to slice up the stylistic variance in PD will be necessarily questionable and temporary. For this reason, it is wise that the *DSM-5* is being conceived of as a living document subject to ongoing empirical and conceptual refinement (Krueger, Eaton, Derringer, et al., 2011). From our perspective, the process for making decisions about which PD constructs are sufficiently valid for routine clinical consideration should be regarded as a psychometric matter (Loevinger, 1957).

The PDs listed in the *DSM-IV* and its appendix offer a reasonable starting point as a list of hypothetical constructs in the PD domain (MacCorquodale & Meehl, 1948). The first step in establishing their construct validity would involve describing their theoretical contents thoroughly. Next, these contents would be measured using multiple assessment methods in diverse samples. The constructs would then be refined based on the psychometric considerations, including (a) replicability of factor structure; (b) discriminant validity relative to one another, personality pathology, and normative traits; (c) freedom from bias; (d) reliability; and (e) criterion validity. Clinically efficient methods for their assessment would then be developed and field tested, permitting subjugation to further refinement through psychometric procedures. Ideally, the resulting constructs would provide a means for developing a coherent theory of PD style that could facilitate clinical formulations, future research, and testable inferences about dynamic processes.

Several investigators have undertaken projects along these lines, leading to the development of Clark's (1993) *Schedule for Nonadaptive and Adaptive Personality*, Livesley and Jackson's (2006) *Dimensional Assessment of Personality Problems*, and the *DSM-5* trait proposal (Krueger, Eaton, Clark, et al., 2011). This line of work provides an important foundation for the process of depicting PD and delineates areas needing further study. For example, because all of these research programs have relied nearly exclusively on self-report questionnaires, which may be limited in some respects for assessing PD (Huprich & Bornstein, 2007), future investigations should employ multiple assessment methods. Second, variance in the structure of each of these models needs to be resolved to build consensual models of PD. Third, each of these models has been guided by an underlying trait perspective on PD classification, and the integration of these approaches with other theoretical approaches, including those that emphasize dynamic or potentially discontinuous aspects of PD or that separate personality pathology from PD, remains unclear.

THE SEPARATION OF PERSONALITY PATHOLOGY AND DISORDER

Separating severity and style, as is done in *DSM-5* Section III, has the potential to improve diagnostic efficiency and predictive validity. This two-part model of personality pathology and PD is analogous to common conceptions of intelligence involving a general component (i.e., *g* or IQ) and specific components (e.g., verbal versus nonverbal abilities). Clinical diagnosis is determined by the standing on the general component; just as mental retardation is defined by a particularly low IQ score, the diagnosis of personality pathology could be defined by a particularly low score on a measure of general personality functioning. More specific predictions about impairment can be made when severity and stylistic elements are distinguished. For example, clinicians would predict that any individual with intellectual disabilities would do poorly in schoolwork relative to most other students, but they would further predict that individuals with personal strengths in verbal versus nonverbal abilities would perform relatively better in reading than mathematics classes. Analogously, severity of personality pathology may permit predictions about the overall level of treatment needed (e.g., inpatient versus outpatient), whereas PD style permits

predictions about how pathology will manifest (e.g., as impulsive social behavior or social withdrawal) and what treatment techniques might be most effective (e.g., group versus individual therapy, pharmacotherapy).

One general issue that requires reconciliation in distinguishing personality pathology severity from style involves their differential association with some PD constructs. Specifically, the terms *borderline* and *narcissism* are treated as distinct disorders in the *DSM-IV*, but they have historically been employed as a general term for personality pathology in several major theories (e.g., Kernberg, 1984; Kohut, 1971). Indeed, empirical models of personality organization appear to relate, conceptually and empirically, to these two PDs (Morey, 2005; Morey et al., 2011). So are narcissistic and borderline PDs discrete, stylistic elements of PD, or are they proxies for personality pathology? These are the kinds of theoretical questions that require resolution through empirical procedures if the field is to make progress toward a more scientifically valid and clinically useful model of personality pathology and disorder. We will return to contemporary issues in PD classification at the end of the chapter. First, we review the historical context of current operationalizations and empirical evidence relating to the prevalence, etiology, and course of PDs as defined by the *DSM-IV*.

DIAGNOSTIC CONSIDERATIONS: A HISTORICAL BACKDROP TO THE DSM-IV

Clinicians have been interested in pathological manifestations of personality for as long as they have been deriving psychopathology taxonomies. Among the first material approaches on record occurred in the fourth century B.C., when Hippocrates translated the philosophies of ancient Mesopotamia (Sudhoff, 1926) into a taxonomy consisting of four temperaments that he believed corresponded to imbalance in bodily humors: choleric (irritable), melancholic (sad), sanguine (optimistic), and phlegmatic (apathetic). It is notable how similar these temperaments are to contemporary models of human personality (i.e., irritable ~ disagreeable, sad ~ neurotic, sanguine ~ extraverted, and phlegmatic ~ [un]conscientious). Hippocrates developed a taxonomy for psychiatric conditions based on these temperamental factors and other conditions, which included six classes of disease: phrenitis, mania, melancholia, epilepsy, hysteria, and Scythian disease (Menninger, 1963). Clinical theorists such as Galen added complexity to early Greek models throughout the Middle Ages and Renaissance, but the quasi-medical approach to classification and basic categories remained fairly similar and continued to be influenced somewhat by supernatural assumptions.

In the 17th century, scientific approaches began to supplant concepts that were rooted in clinical descriptions colored by metaphysical theories. The enhanced focus on falsifiable methods from the 17th century onward paved the way for contemporary models in descriptive psychiatry. Emil Kraepelin, who produced nine volumes of clinical psychiatry textbooks from 1883 to 1927 that represented a standard text on psychiatric classification during his lifetime and for many years to follow, is widely regarded as the pioneer of this movement. The aspect of his approach that set him apart from previous theorists was his focus on the course of disorders, in addition to

their signs and symptoms. The concept of course is particularly important for PDs, which have been distinguished from other disorders based on the presumption that they are relatively more enduring. Given his focus on course and the historical importance of personality pathology, it is not surprising that many of the concepts in Kraepelin's textbook are easily identified in the *DSM* PDs. This link is also due to Kraepelin's influence on early 20th-century efforts to categorize mental disorders in the United States (Menninger, 1963). In the middle of that century, Kraepelinian concepts were blended with psychoanalytic ideas by major figures such as Adolf Meyer and William Alanson White, who contributed significantly to the conceptual models of psychopathology underlying the first *DSM*.[1]

DSM-I AND DSM-II

PDs have appeared in every edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*; American Psychiatric Association [APA], 1952, 1968, 1980, 1987, 1994, 2000). In the *DSM-I,* they were characterized by developmental defects or pathological trends in personality structure, with minimal subjective anxiety and little or no sense of distress. In most instances, the disorder is manifested by a lifelong pattern of action or behavior, rather than by mental or emotional symptoms (APA, 1952, p. 34). These three pillars of PD definition have persisted in subsequent editions: PDs are thought to be developmental, stable, and ego-syntonic.

The *DSM-I* employed a narrative rating system for diagnosing PDs, meaning that clinicians were expected to determine a diagnosis based on the perceived match between a patient's behavior and a description of pathological prototypes in the manual. PDs in *DSM-I* were separated into distinct groups. Personality pattern disturbances were regarded as "deep-seated," "with little room for regression." These included the inadequate, schizoid, cyclothymic, and paranoid types. Personality trait disturbances referred to conditions brought about by stress, which were thought to indicate latent weaknesses in the underlying personality structure. These included emotional instability, passive aggression, compulsivity, and an "other"category. Sociopathic personality disturbances were similar to personality trait disturbances, but their manifestation was thought to be driven primarily by a mismatch between an individual's behavior and cultural norms. Such disturbances included antisocial and dyssocial reactions, sexual deviance, and substance abuse.

Although the second edition of the *DSM* (APA, 1968) brought with it some theoretical and classificatory changes to the PDs, it remained very similar in underlying approach and in content to the first edition. The primary change was the removal of the three diagnostic subcategories in favor of the more straightforward depiction of 10 distinct types, largely carried over from *DSM-I*. Specifically, dependent and aggressive subtypes of passive aggressive personality were collapsed, compulsive personality was reconceptualized and renamed obsessive-compulsive personality, dyssocial personality was renamed explosive personality, and asthenic personality, conceptualized as involving dependency and compromised character strength, was added. Finally, although PDs continued to be differentiated from other disorders in terms of their supposed ego-syntonicity, the assertion that patients with PDs routinely did not experience distress as a result of their personality pathology was tempered (Oldham, 2005).

DSM-III AND *DSM-IV*

In order to improve diagnostic reliability, *DSM-III* categories were rated based on atheoretical, behavioral symptom criteria rather than prototype descriptions that were rooted in the formulations of specific theories and required relatively more clinical inference. The *DSM-III* also introduced the multiaxial system, in which a distinction was made between Axis I conditions (thought to be acute, ego-dystonic, and relatively amenable to treatment) and Axis II conditions (thought to be enduring, ego-syntonic, and relatively resistant to treatment), with PDs belonging to Axis II. Four *DSM-II* PDs were either eliminated (inadequate and asthenic) or moved to Axis I (cyclothymic and explosive). Schizoid PD was separated into schizoid (defined by interpersonal aloofness), schizotypy (defined by odd behavior), and avoidant (defined by fear of interpersonal criticism/embarrassment) PDs. Two new PD diagnoses, borderline and narcissistic, were introduced in *DSM-III*. Finally, the PDs were grouped into three clusters based on their degree of shared phenomenology: Cluster A consisted of schizoid, schizotypal, and paranoid; Cluster B of borderline, histrionic, narcissistic, and antisocial; and Cluster C of obsessive-compulsive, avoidant, dependent, and passive-aggressive.

The *DSM-IV* largely retained this system, with three major exceptions: (1) the antisocial criteria were simplified somewhat; (2) a paranoid/dissociation criterion was added to borderline; and (3) passive-aggressive PD was appendicized. The rationale for removing passive-aggressive PD was that it referred to a narrow behavioral tendency, rather than a broad personality syndrome (Millon & Radovanov, 1995), although this view has been challenged on rational (Wetzler & Morey, 1999) and empirical (Hopwood et al., 2009) grounds. Finally, personality pathology was formally operationalized, separately from the criteria of each specific PD. It was defined as (a) an enduring pattern of inner experience and behavior that deviates markedly from the expectations of the individual's culture and is manifested in at least two of the following areas: cognition, affectivity, interpersonal functioning, or impulsive control; (b) pervasive across a broad range of personal and social situations; (c) leading to clinically significant impairment in social, occupational, or other important areas of functioning; (d) stable with an onset that can be traced back at least to adolescence or early adulthood; (e) not better accounted for by another mental disorder; and (f) not due to the direct physiological effects of a substance or medical condition. Criteria sets were polythetic for all PDs, whereas in the *DSM-III* criteria for some PDs had been more typological and impressionistic due to limited theoretical and empirical understanding. For example, a patient would have to meet all three of the *DSM-III-R* dependent PD criteria for the diagnosis, including passively allowing others to assume responsibility, subordinating needs to others, and lacking self-confidence. In the *DSM-IV*, a patient would need to meet five of eight symptoms, including difficulties initiating projects on one's own and urgently seeking new relationships for support when old relationships end. While this change enhanced the reliability of the PDs (Pfohl, Coryell, Zimmerman, & Stangl, 1986), the increased use of polythetic criteria may have also worsened the problems of construct heterogeneity and diagnostic overlap (Gunderson, 2010).

CLINICAL PICTURE: THE *DSM-5* SECTION II PERSONALITY DISORDERS

Having described the clinical importance of personality pathology, defined the central concepts of personality and related pathology, and reviewed the history of PD taxonomy, we will now focus on clinical manifestations of the PDs listed in Section III of *DSM-5* (APA, 2013). Cluster A consists of paranoid, schizoid, and schizotypal PDs, which are thought to share odd and eccentric features. These disorders are associated with psychotic disorders phenomenologically and etiologically (Maier, Lichtermann, Minges, & Heun, 1994) but are distinguished by their lack of persistent psychotic symptoms (i.e., hallucinations and delusions). *Paranoid* PD is defined by a pervasive pattern of distrust and beliefs that others' motives are malevolent. Symptoms involve suspiciousness and consequent social dysfunction, loose and hypervigilant thinking, and resentment. *Schizoid* PD is characterized by a pervasive pattern of social detachment and restricted emotional expression. Symptoms include disinterest in relationships and preference for solitude, limited pleasure in sex or other activities commonly regarded as pleasurable, and emotional flatness. The defining feature of *schizotypal* PD is a pervasive pattern of interpersonal deficits, cognitive or perceptual distortions, and eccentric behavior. It is diagnosed by symptoms related to loose or eccentric perceptions and cognitions, flat affect, mistrustfulness, and profound social dysfunction.

Antisocial, borderline, histrionic, and narcissistic PDs constitute Cluster B, which is regarded as the "dramatic, erratic, and emotional" group (APA, 2000). Individuals with these disorders tend to experience emotional dysregulation and behave impulsively. *Antisocial* PD is marked by a pervasive pattern of disregard for the rights and wishes of others (APA, 2000). The *DSM-IV* requires evidence of childhood conduct disorder for a diagnosis of antisocial PD, and additionally includes symptoms of socially nonnormative behavior, dishonesty, impulsivity, aggression, lack of empathy, and irresponsibility. *Borderline* PD is characterized by "stable instability" (Schmideberg, 1959) in emotions, interpersonal behavior, and identity. Emotional dysregulation, including anger and emptiness, is thought to be triggered by concerns about abandonment, which is followed by maladaptive coping, including impulsive and suicidal behavior (Zanarini & Frankenburg, 2007). *Histrionic* PD is characterized by excessive emotionality and attempts to obtain attention from others. This desire to be the center of attention often comes at the cost of deep and meaningful interpersonal relationships, as histrionic individuals tend to have relatively superficial interpersonal interactions and shallow emotions. The core of *narcissistic* PD involves grandiose thoughts and behaviors, a need for excessive admiration from others, and a lack of empathy. It is commonly believed that arrogant and haughty behavior is undergirded by feelings of vulnerability and inadequacy.

Cluster C includes avoidant, dependent, and obsessive-compulsive PDs, which are grouped together based on their common thread of anxiety and fearfulness. *Avoidant* PD is characterized by social inhibition rooted in feelings of inadequacy and fears of negative evaluations from others (APA, 2000). Symptoms include avoidance of social and occupational opportunities, fears of shame and ridicule, and negative self-concept. *Dependent* PD is defined by an excessive need to be cared for by others that leads to submissive, clingy behavior. Symptoms include difficulties making autonomous decisions or expressing disagreement with others,

nonassertiveness, preoccupation with abandonment, and maladaptive or self-defeating efforts to seek and maintain relationships. *Obsessive-compulsive* PD is defined by a preoccupation with order, perfection, and control in which flexibility, efficiency, and even task completion are often sacrificed. Symptoms include preoccupation with rules and order, perfectionism, workaholism, interpersonal inflexibility, frugality, and stubbornness.

RESEARCH ON THE *DSM-5* SECTION II PERSONALITY DISORDERS

Epidemiology

One of the principal advantages of the *DSM-III* and *DSM-IV* model of PDs that is being carried over to *DSM-5*, Section II has been its contribution to the increase in PD research. However, to the extent that a majority of this research has been based on a flawed conception of PDs, its utility is constrained by the validity of the model. Epidemiology instantiates this paradox. Although the development of reliable PD criteria has made it more possible to evaluate the prevalence of PDs, calculating the prevalence of PDs assumes that they are categorical taxa, even though the weight of evidence suggests they are not (Trull & Durrett, 2005), and diagnostic cutoffs in the *DSM-IV* are thus essentially arbitrary (Cooper, Balsis, & Zimmerman, 2010). As such, it is not clear what to make of PD prevalence rates. With this caveat in mind, we review the results of several epidemiological studies on PD based on *DSM* diagnostic cutoffs.

Overall prevalence rates estimate that more than 10% of individuals suffer from a PD during their lifetime (Grant et al., 2004; Lenzenweger, Loranger, Korfine, & Neff, 1997; Samuels et al., 2002; Torgersen, 2005; Torgersen et al., 2001). Although rates for individual PDs are more variable across studies, research suggests that most PDs have prevalence rates between 0.5% and 5%, with paranoid, avoidant, and obsessive-compulsive PDs being relatively common and dependent and narcissistic PDs being relatively uncommon. PD prevalence is considerably higher in psychiatric settings: Research indicates that nearly half of clinical outpatients and more than half of clinical inpatients meet the diagnostic criteria for a PD (Molinari, Ames, & Essa, 1994; Zimmerman, Rothschild, & Chelminski, 2005), making PDs among the most commonly encountered disorders in psychiatric settings. The two most commonly occurring PDs among psychiatric patients are borderline, 10% to 20% (APA, 2000; Zimmerman et al., 2005), and dependent PD. Rates of dependent PD are particularly high among inpatients, 15% to 25% (Jackson et al., 1991; Oldham, 2005), relative to outpatients, 0% to 7% (Mezzich, Fabrega, & Coffman, 1987; Poldrugo & Forti, 1988; Zimmerman et al., 2005).

In contrast, somewhat lower occurrence rates have been observed for paranoid (2% to 4%; Zimmerman et al., 2005), schizoid, and schizotypal (1% to 2%; Stuart et al., 1998; Zimmerman et al., 2005) patients in clinical settings. These relatively low rates may relate to the impact of the paranoia and social avoidance that characterizes these disorders on treatment seeking. Indeed, prevalence estimates for schizoid PD among a homeless population are as high as 14% (Rouff, 2000). Likewise, antisocial PD is seen in 1% to 4% of individuals in a clinical population (Zimmerman et al., 2005), but estimates are considerably higher in prison and substance abuse

populations, indicating that individuals with this type of pathology are unlikely to initiate psychological treatment. Somewhat low rates have also been observed for narcissistic (2%; Torgersen et al., 2001) and obsessive-compulsive (3% to 9%; Zimmerman et al., 2005) PDs in clinical settings, perhaps owing to the limited functional impact of these PDs relative to others. Rates of histrionic and avoidant PD in clinical patients have been estimated at 10% to 15% (APA, 2000; Zimmerman et al., 2005).

ETIOLOGY

Despite extensive theorizing, empirical evidence regarding the etiology of PDs is quite limited (Paris, 2011; Skodol et al., 2011). Factors contributing to this gap between theory and evidence include a history of underfunding for PD research relative to research on other psychiatric conditions and various conceptual problems discussed throughout this chapter. Nevertheless, we briefly review etiological contributions related to genes, neurobiology, learning, and cognition presently.

Genetics While the broad heritability of personality traits is well-established (McGue, Bacon, & Lykken, 1993; Plomin, DeFries, Craig, & McGuggin, 2003), the heritability of personality pathology and disorders remains more ambiguous (Lenzenweger & Clarkin, 2005). A twin study by Torgersen and colleagues (2000) indicated that the overall 58% of the variance in PDs was due to genes, with specific heritability estimates for each PD as follows: paranoid (0.30), schizoid (0.31), schizotypal (0.62), borderline (0.69), histrionic (0.67), narcissistic (0.77), avoidant (0.31), dependent (0.55), and obsessive-compulsive (0.78). Notably, shared family environment influences were also particularly important in predicting borderline PD. These results led the authors to conclude that PDs may have even stronger genetic influences than most other disorders, similar to broad dimensions of normative personality. Rates of antisocial PD were too low to be included in the Torgersen et al. (2000) study; however, work by other researchers has broadly evidenced that the heritability of aggression is between 44% and 72% (Siever, 2008). A meta-analysis suggests the importance of both genetic and environmental influences on antisocial behavior in men and women, though this influence was measured on antisocial behaviors as opposed to antisocial PD (Rhee & Waldman, 2002). Evidence also suggests higher rates of schizotypal (Kendler et al., 2006) and borderline (Links, Steiner, & Huxley, 1988) PDs among family members of individuals with those disorders, and increased rates of Cluster C PDs among individuals who have relatives with Axis I anxiety disorders (Reich, 1991).

Evidence also suggests interactive effects between genes and the environment, such as the finding that associations between a polymorphism on the MAOA gene is associated with antisocial traits only in individuals who have been exposed to trauma (Caspi et al., 2002). Evidence suggesting an interaction between genes and the early attachment environment may also be crucial in subsequent development of PDs (Siever & Weinstein, 2009). The interplay of genes and environment in the genesis of psychopathology is quite complicated (e.g., Burt, 2009), and much more research is needed with respect to the etiology of PDs. Beyond a basic decomposition of the etiological components of personality pathology and specific PDs, research should

begin focusing more on molecular models and the interplay between behavior genetic and environmental risk factors.

Neurobiology As with etiology and despite a recent rise in interest in understanding neurological risk factors for the development of PDs (for a review, see Siever & Weinstein, 2009), potential neurobiological endophenotypes for PDs are largely unknown (Paris, 2011; Skodol et al., 2011). It is widely presumed that endophenotypes are more likely to reflect neurobiological dimensions that underlie personality pathology rather than point to pathways to specific PDs. Potential dimensions include those related to cognitive dysregulation, impulsivity, and emotional dysregulation (Depue & Lenzenweger, 2005; Siever & Weinstein, 2009). We will briefly review these three classes of potential endophenotypes and their implications for PDs.

Cluster A PDs, and particularly schizotypal, share features of *cognitive dysregulation* with schizophrenia, including distorted perception and disrupted attention. Cognitive dysregulation is thought to relate to reduced dopamine reactivity in the frontal cortex (Abi-Dargham et al., 1998; Seiver & Weinstein, 2009), as well as structural anomalies found in psychotic disorders such as increased ventricular volume (Hazlett et al., 2008). The influence of common endophenotypes represents a promising explanation for descriptive and phenomenological similarities between Cluster A PDs and psychotic disorders (Depue & Lenzenweger, 2005).

Impulsivity is a reaction to emotional provocation, implicating a failure in higher-order mental processes that may predispose several PDs, and particularly those in Cluster B (Siever & Weinstein, 2009). Indeed, there is evidence of reduced cortical activation during impulsive behavior (New et al., 2004) and evidence that serotonin plays an important mediating role in the top-down regulation of impulsive, and particularly aggressive, impulses (Brown et al., 1982; Coccaro, Gabriel, & Siever, 1990; Winstanley, Theobald, Dalley, Glennon, & Robbins, 2004) generated from limbic structures (Herpertz et al., 2001).

Emotional dysregulation is also related to Cluster B PDs, and it often takes the form of aggressive behavior, making it difficult to distinguish descriptively from impulsivity. Emotional dysregulation is associated with amygdala hyperreactivity (Donegan et al., 2003; Herpertz et al. 2001), suggesting that it may be dynamically related to impulsive behavior: Hypersensitivity to threat leads to emotional dysregulation, and failure to modulate the urge to act based on dysregulated emotion by cortical structures leads to impulsive, often aggressive, behavior. Anxiety is thought to underlie Cluster C PDs, which are responsive to chemical manipulations of serotonin and dopamine (Schneier, Blanco, Anita, & Liebowitz, 2002), suggesting common endophenotypes with mood and anxiety disorders (DeYoung, 2010).

Learning and Cognition A large body of theory and empirical evidence supports links among attachment patterns, developmental trauma, and PDs. In particular, attachment patterns are related to the stylistic expression of PD (Meyer & Pilkonis, 2005), and childhood maltreatment is associated with the development of personality pathology in general (Johnson, Cohen, Brown, Smailes, & Bernstein, 1999) and some PDs specifically (e.g., borderline; Zanarini, Gunderson, Marino, & Schwartz, 1989). Several theories have been organized specifically around the interpersonal antecedents of personality pathology. For instance, Benjamin (1996) has formulated each of the

DSM-IV PDs in terms of specific and testable developmental patterns. She has also outlined a broad framework for conceptualizing developmental "copy processes" that could usefully inform research in this area (Critchfield & Benjamin, 2010). Unfortunately, research is currently too limited to speak with confidence regarding the interpersonal mechanisms that generate or maintain PD; more research is certainly needed on this important but neglected issue.

Cognitive theorists implicate three fundamental aspects of cognition in the development of PDs: automatic thoughts, cognitive distortions, and interpersonal strategies (Pretzer & Beck, 2005). From this perspective, individuals apply automatic (i.e., implicit or unconscious) thoughts to events they encounter that are rooted in deep-seated ways of interpreting the world, learned in early childhood. For some individuals, these automatic thoughts may lead to cognitive distortions, which, in turn, result in maladaptive interpersonal strategies that reinforce and maintain an individual's personality pathology. Several automatic thoughts and cognitive distortions have been hypothesized for specific PDs (Beck & Freeman, 1990). For example, individuals with avoidant PD may be prone to automatic thoughts such as "I am incompetent, " whereas individuals with obsessive-compulsive PD are more likely to employ dichotomous thinking (Beck & Freeman, 1990). As with interpersonal models, further research is needed on cognitive models of the genesis and maintenance of personality pathology.

Course and Prognosis

According to the *DSM-5*, individuals cannot be diagnosed with personality pathology before age 18, even though pathological personality features should be present during adolescence and early adulthood for a diagnosis during adulthood. This definition is sensitive to the ill-formed nature of personality during the transition to adulthood (Arnett, 2000) and the possibility that personality problems in childhood may reflect developmental challenges that would remit with maturity (although see Shiner, 2009). There is no upper restriction on PD diagnosis in the *DSM-5*, but most PDs tend to decline in middle age (although see Tackett, Balsis, Oltmanns, & Krueger, 2009). As such, PDs as conceptualized in the *DSM-5* Section II can generally be regarded as disorders of young to middle adulthood. Within this period, PDs have long been presumed to be stable and pervasive. This assumption has caused significant skepticism regarding prognosis. However, recent research suggests some optimism for therapeutic improvement in that the stability of PDs seems to be lower than was once thought, and treatments have shown benefit for at least some PD symptoms. This research and its implications for conceptualizing personality pathology are discussed presently.

Course Several longitudinal studies of PD in adult clinical samples in the past few decades have shed significant light on the course of PDs (Morey & Hopwood, 2013). The Collaborative Longitudinal Personality Disorders (CLPS) study followed individuals with PDs or major depression for 10 years. Early research from this study found that PDs declined rapidly over the first 2 years of follow-up (Grilo et al., 2004). Later research showed that PD features were less stable than personality traits (Morey et al., 2007), and that some PD features declined more rapidly than others (McGlashan

et al., 2005), leading to the proposal that personality pathology reflects a hybrid combination of stable, enduring personality traits and dynamic, environmentally contingent symptoms. Zanarini's McLean Study of Adult Development (MSAD) is an ongoing study that has followed individuals with borderline PD and a comparison clinical sample without borderline PD for more than 16 years. As in CLPS, remission from borderline PD was more rapid than anticipated in the MSAD (Zanarini, Frankenburg, Hennen, Reich, & Silk, 2007), and again temperamental and acute symptoms were identified (Hopwood, Donnellan, & Zanarini, 2010; Zanarini et al., 2007). Lenzenweger's Longitudinal Study of Personality Disorder similarly showed, in a college student sample followed for 4 years, that there exists "compelling evidence of change in PD features over time and does not support the assumption that PD features are trait-like, enduring, and stable over time" (Lenzenweger, 2006, p. 662).

Overall, these findings suggest that some aspects of personality pathology are stable, as has been historically assumed, whereas other aspects appear to operate more like the symptoms of Axis I disorders: They are malleable and perhaps reactive to the influence of environmental dynamics. Thus it may be possible, diagnostically, to distinguish aspects of PD that are due to temperamental diatheses from those that are due to dynamic environmental processes, or the interaction between traits and contexts. These promising findings also suggest that some aspects of PD may be subject to change through psychological treatment, a topic to which we now turn.

Treatment Effects There is limited evidence that psychopharmacology is effective for treating PD, with results mostly suggesting that targeted use of medication may benefit certain symptom constellations (e.g., the emotional lability of borderline PD or the cognitive slippage of schizotypal PD; Siever & Weinstein, 2009) but not treat the totality of PD symptoms. Nevertheless, polypharmacy for PDs is common (Zanarini, Frankenburg, Hennen, & Silk, 2004). Perhaps in part because of the longstanding belief that PDs are intractable, relatively few psychosocial treatments have been developed for personality pathology, and most of them have been developed for a single disorder, borderline PD (Matusiewicz et al., 2010). Several issues complicate the effectiveness of psychosocial treatments, including relatively high rates of early dropout (particularly in BPD, c.f. Skodol, Buckley, & Charles, 1983), substantial diagnostic complexity (McGlashan et al., 2000), and the tendency for PD treatment to be unpleasant for clinicians, who may consequently exhibit iatrogenic behavior.

That said, some headway is being made with regard to borderline PD, with several treatments showing benefit in controlled research, including dialectical behavior therapy (Linehan, 1993), transference-focused therapy (Clarkin, Levy, Lenzenweger, & Kernberg, 2007), schema-focused therapy (Giesen-Bloo et al., 2006), psychiatric management (Gunderson, 2008), and mentalization-based therapy (Bateman & Fonagy, 2004). It is notable that these therapeutic models come from very different theoretical backgrounds, yet they share several features, including a highly structured therapeutic frame, a focus on the relationship between therapist and client, and a focus on managing self-damaging behavior through contracting and explicit crisis plans. The treatments also tend to show similar effects in controlled research (Clarkin et al., 2007). One potential conclusion to draw from the similarity of these treatments is that, in dealing with complex phenomena such as PDs, it is more helpful to integrate the

wisdom of multiple perspectives than to cling to theoretical dogma. This lesson may fruitfully translate to the issue of PD classification, to which we now turn.

ASSESSMENT

The manner in which personality pathology and PD are assessed varies across theoretical and measurement approaches, with preferences for particular methods often being related to underlying theoretical assumptions. Common assessment methods are thus organized as follows according to their underlying theoretical foundation. Specifically, we distinguish *DSM*-based, trait, and psychoanalytic approaches to the assessment of personality pathology and PD.

DSM

The most common and widely accepted method for assessing personality pathology and PD involves translating the *DSM* PD symptoms into questions that individuals can endorse, and then determining whether they meet criteria based on the number of symptoms endorsed. Assessing PDs based on *DSM* symptoms can occur either via interview or questionnaire; clinicians tend to prefer unstructured interviews, whereas researchers tend to prefer semistructured interviews or self-report inventories (Widiger & Samuel, 2005). Structured and semistructured interviews are more reliable than unstructured interviews (Rogers, 2001), but unstructured interviews may have the advantages of allowing dynamics between patients and clinicians to occur more naturally and of not requiring patients to have insight into their own personality pathology (Westen, 1997). Conventionally, clinician or research interviews have been regarded as the criterion method for determining whether an individual has a PD. This is partially based on the belief that clinicians are better able to infer meanings and motivations behind client behaviors than individuals with PDs, who are commonly thought to lack insight regarding their pathology.

Numerous measures exist for assessing PDs using the *DSM* model (Widiger & Samuel, 2005). Among the more commonly employed instruments are the clinician-administered *Structured Clinical Interview for DSM-IV TR Axis II Personality Disorders* (SCID-II; First, Gibbon, Spitzer, Williams, & Benjamin, 1997) and the self-report *Personality Disorder Questionnaire* (Hyler, 1994). Given that rates of PD are lower by interview than self-report (Clark & Harrison, 2001; Hopwood et al., 2008), a method advocated by First et al. (1997) and others is to screen for PDs using a self-report questionnaire and then use a clinician-administered semistructured interview as a follow-up procedure to determine whether an individual meets diagnostic criteria for disorders endorsed by self-report.

A primary advantage of the *DSM* symptom-based method is that it provides a consensual way to evaluate PDs and thus increases confidence among clinicians and researchers that they are assessing the same constructs. However, agreement among DSM-based measures is poor (Skodol, Rosnick, Kellman, Oldham, & Hyler, 1991), and assessing PDs from the *DSM* perspective is limited to the degree that the *DSM* model is of questionable validity, as many have suggested. Several authors have argued that a more theoretically coherent model is needed to improve methods for assessing

personality pathology and disorders. Trait and psychoanalytic models, which are described as follows, may offer desirable theoretical coherence.

Trait Models

Building upon consistent evidence that personality traits such as those of the FFM systematically relate to *DSM* PDs (Samuel & Widiger, 2008; Saulsman & Page, 2004), trait researchers have developed methods for deriving PD scores from FFM-based assessments (Miller, Bagby, Pilkonis, Reynolds, & Lynam, 2005). A potential advantage to FFM assessment methods is that normal and pathological personality can be evaluated within the same model. This would permit, for example, an assessment of personality strengths that may not be afforded by an exclusive focus on PD constructs (Samuel, 2011). However, one potential limitation to this approach is the possibility that normative measures such as those based on the FFM do not effectively assess some important aspects of personality pathology and disorder (Hopwood, 2011; Krueger, Eaton, Derringer, et al., 2011; although see also Haigler & Widiger, 2001). It is also possible that the self-report method, on which most trait research relies heavily, may be limited for some aspects of personality pathology assessment (Huprich & Bornstein, 2007).

A related approach to PD assessment involves focusing on maladaptive traits rather than general personality, as in the FFM. The two predominant measures that are used in this regard are the *Dimensional Assessment of Personality Pathology* (Livesley & Jackson, 2006), which was initially developed to test the structure of the *DSM* model but later reformulated as a trait model, and the *Schedule for Nonadaptive and Adaptive Personality* (Clark, 1993), which was developed to provide a means for dimensionally assessing clinically relevant personality and personality pathology traits. Both measures consist of higher-order factors that resemble subsets of FFM traits (Widiger, Livesley, & Clark, 2009) and lower-order factors that assess pathological personality traits. Recently, Krueger and colleagues have developed a questionnaire that is similar to these measures to serve as the basis for pathological trait assessment in the *DSM-5* (Krueger et al., 2011a, 2011b, 2012).

Psychoanalytic Assessment

Unlike trait psychologists, psychoanalytically oriented clinicians and researchers tend to prefer clinician ratings or performance-based assessment over self-report methods. There has also been increased interest among psychoanalytic researchers and clinicians in using prototypes to assess PDs. The *Shedler and Westen Assessment Procedure* (SWAP; Westen & Shedler, 1999) is a prototype-based clinician rating method informed by psychoanalytic theory. On the SWAP, clinicians describe their patients' personalities by sorting 200 cards that are applicable to varying degrees to the patient being rated. These sorts can then be compared with prototypes to determine the most likely diagnosis. Evidence suggesting that clinicians tend to think of patients in prototypical terms rather than trait profiles (Rottman, Woo-kyoung, Sanislow, & Kim, 2009; Westen, Shedler, & Bradley, 2006) makes the SWAP and similar procedures appealing. However, prototypes are not without limitations, mainly owing to their potential unreliability (Zimmerman, 2011) and the

loss of information that occurs when ratings are made globally (Samuel, Hopwood, Krueger, Thomas, & Ruggero, 2013). For instance, if a patient is a good match to a given prototype, that could either mean the patient moderately matches nearly all features of the description or matches some features of the description extremely well and others not so well.

Another approach involves using measures that assess features of psychoanalytic theories that deviate from the *DSM* model. For instance, psychoanalysts have developed the *Psychodynamic Diagnostic Manual* (PDM Task Force, 2006; see also *Journal of Personality Assessment* special issue 2, 2011) for this purpose. Other examples include the *Structured Interview of Personality Organization* (Stern et al., 2010) and the *Inventory of Personality Organization* (Kernberg & Clarkin, 1995), which are based on Kernberg's (1984) model of personality pathology. An appealing feature of this model is that it explicitly separates personality pathology (i.e., personality organization) from PDs. However, thus far these measures have been subjected to limited psychometric research.

A third historically psychoanalytic approach to assessing personality pathology involves performance-based assessment methods in which individuals provide open-ended responses to novel stimuli. For example, the *Rorschach Inkblot Method* (Huprich, 2005), in which individuals describe what images they see in a series of inkblots, the *Thematic Apperception Test*, in which individuals produce stories to go along with pictures, and sentence completion tests (e.g., Hy & Loevinger, 1996) are commonly employed performance-based assessments. Scoring methods have also been developed to score patient narratives as a way of evaluating concepts that are important in psychoanalytic theory, such as defense mechanisms (Cramer, 1991) and the quality of object relations (Westen, 1995).

The primary strengths of psychoanalytic approaches to PD assessment include that they are embedded in a coherent theory of personality pathology and that they may be better suited than interviews and self-reports for identifying pathological personality processes that are outside of individuals' awareness (Huprich & Bornstein, 2007). However, there is limited empirical support for psychoanalytic approaches to PD assessment relative to *DSM*-based and trait assessment instruments, and using methods that are informed heavily by nonconsensual theories risks returning to a time when clinicians used the same terms to mean different things. Furthermore, clinician ratings and performance-based methods are time-consuming relative to questionnaires. Thus, the utility of psychoanalytic approaches could be better judged if they were made as efficient as possible and linked better empirically to other approaches to PD assessment.

SUMMARY

Overall, any assessment method designed to evaluate complicated constructs such as personality pathology and PDs is likely to have strengths and weaknesses. The optimal strategy is therefore to use multiple assessment methods from varying theoretical perspectives. One example of a more comprehensive approach is the LEAD standard (Pilkonis, Heape, Ruddy, & Serrao, 1991), in which all available current and historical data from any methods are evaluated by a team of expert clinicians to derive the most reliable possible diagnosis.

THE *DSM-5*

Personality pathology is significantly reconceptualized in the *DSM-5* Section III (Skodol et al., 2011). It is likely that something like this reconceptualization will ultimately replace the problematic *DSM-5* Section II model in future versions of the *DSM*. In this section, we describe widely recognized problems with the *DSM-IV* model that led to this reconceptualization, the *DSM-5* Section III alternative, and the impact of the *DSM-5* on scientific validity and clinical utility. We conclude by highlighting differences between the *DSM-5* Section II and III approaches to PD diagnosis with a case study.

Criticisms of the *DSM-5* Section II PDs

Although the Section II model, derived from *DSM-III* and *DSM-IV*, has catalyzed PD research, the research it has stimulated has contributed to the identification of several limitations of the system (Clark, 2007). Many limitations relate to the categorical conceptualization of PD, which appears to fit nature poorly (Trull & Durrett, 2005), worsens reliability (Heumman & Morey, 1990), and necessitates arbitrary diagnostic cutoffs (Skodol et al., 2011). Others, such as profound diagnostic overlap (Clark, 2007; Oldham, Skodol, Kellman, Hyler, & Rosnick, 1992) and the common use of a not-otherwise-specified category (Verheul & Widiger, 2004), appear to relate to the questionable empirical structure of the PDs (Hopwood et al., 2011). The polythetic format of PD criteria (Krueger, Eaton, Derringer, et al., 2011), conflation of personality severity and style in PD symptoms (Parker et al., 1998), and the arbitrary diagnostic cutoffs contribute to problematic diagnostic heterogeneity. *DSM-IV* constructs also conflate relatively stable traits with more dynamic symptoms (McGlashan et al., 2005; Zanarini et al., 2007). Finally, as discussed previously, although the *DSM-III* and *DSM-IV* have promoted PD research in general, some PDs are woefully neglected in the research literature, and the *DSM-IV* has not led to the development of effective treatments for most PDs (Widiger & Mullins-Sweatt, 2009).

DSM-5 Section III PDs

The *DSM-5* Section III model was designed to address some of these problems toward improving the scientific validity and clinical utility of PD diagnosis. We will first describe the basic elements of this model. We will then describe the degree to which it improves the scientific validity and clinical utility of PD assessment.

The *DSM-5* Section III model (Krueger, Eaton, Clark, et al., 2011; Morey et al., 2011; Skodol et al., 2011) includes a general definition of personality pathology which is quantified, six PDs defined by a mix of symptom deficits and pathological traits, and a hierarchical system of pathological traits. The general definition of personality pathology is quantified in terms of levels of functioning on two dimensions rated on a five-point scale: self (i.e., self-definition and autonomy) and interpersonal (i.e., intimacy and empathy). Any patient in the diagnostic range would be assessed for the presence of six potential PDs: antisocial, avoidant, borderline, narcissistic, obsessive-compulsive, and schizotypal; the other four *DSM-IV* PDs (schizoid, paranoid, histrionic, and dependent) have been eliminated. There are five criteria for each PD.

Criterion A involves the core deficits in self and interpersonal functioning that are specific to that disorder. Criterion B lists the traits that are also thought to undergird each disorder. Criteria C through E specify that these features must be stable, deviant, and not better accounted for by other conditions, respectively. Any patient with personality pathology who does meet the criteria for a specific disorder would be classified as PD-trait specified. This specification would be based on a hierarchical model with five higher-order traits (negative affectivity, detachment, antagonism, disinhibition, and psychoticism) and 25 lower-order traits (Krueger, Eaton, Clark, et al., 2011a; Krueger, Eaton, Derringer, et al., 2011, in review). These traits could also be used to supplement PD diagnoses, for instance when a patient meets criteria for a certain PD and has several other significant traits, or to describe a patient without any PD diagnosis but with some pathological traits.

The Scientific Validity of *DSM-5* Section III PDs

The *DSM-5* Section III model appears to improve the scientific validity of PD diagnosis in several respects relative to its predecessor. Research discussed earlier supports the quantification of a general personality pathology factor in terms of levels of functioning, and the contents of this rating scale are based on empirical evidence (Morey et al., 2011) rooted in a large body of theoretical considerations and clinical observations (Bender, Morey, & Skodol, 2011). The PDs that are included retain several concepts such as borderline personality, psychopathy, and schizotypy, with considerable construct validity, and the transition to a more personality-based model of psychopathy (Hare, 1991) improves the definition of that construct considerably. The traits incorporate a dimensional perspective and appear to capture the major traits of other dimensional models (Krueger et al., 2012; Wright et al., 2012), addressing the most common evidence-based critique of the *DSM-IV* PDs.

However, several aspects of the *DSM-5* have been questioned on empirical grounds. Because the model is so new and uses a somewhat novel approach to PD assessment, critics have argued that not enough is known about its validity (Shedler et al., 2010; Zimmerman, 2011). For instance, the content of the retained PD constructs is changing considerably and although initial evidence suggests that the *DSM-5* covers the content described in the *DSM-IV* relatively well (Hopwood et al., 2011), the change from polythetic to absolute criteria may have unintended effects such as significantly lowering the prevalence of the PDs. Some have also questioned whether the proposed trait structure will hold up in future research, particularly since it deviates from other models significantly in its employment of unipolar, as opposed to bipolar, traits (Samuel, 2011). This approach also likely contributes to some odd facet-domain relationships, such as the loading of submissiveness onto negative affectivity (Widiger, 2011, although see also Krueger, Eaton, Clark, et al., 2011).

There is also significant controversy regarding decisions about which PD constructs to retain. The response from the clinical and research community to an initial proposal to delete narcissistic PD (e.g., Pincus, 2011) contributed to the *DSM-5* workgroup's decision to include that disorder in its second proposal. However, paranoid, schizoid, histrionic, and dependent PDs did not return. Individuals with pathology described by these terms in the *DSM-IV* would therefore be trait-specified in the *DSM-5*. Decisions regarding which PDs to retain were based primarily on evidence concerning

the prevalence of these conditions and the overall body of research for each PD (Skodol et al., 2011). However it is predictable that clinicians and researchers would hesitate to delete PDs that they have grown accustomed to. Furthermore, losing both dependent and histrionic PDs means that the *DSM-5* may be limited in its assessment of pathology related to interpersonal warmth and excessive needs for affiliation (Wright et al., 2012), a feature these disorders share (Widiger, 2010) and which are not well-represented in the pathological trait model (Pincus et al., 2011).

The Clinical Utility of *DSM-5* Section III PDs

According to First and colleagues (2004), clinical utility involves the clinician's ability to communicate; select effective interventions; predict course, prognosis, and future management needs; and differentiate disorder from nondisorder to determine who might benefit from treatment. The degree to which the *DSM-5* model improves upon the *DSM-IV* can be evaluated in each of these areas.

In terms of communication, the levels of functioning index and any reduction in diagnostic overlap and construct heterogeneity that results from the move from polythetic to type diagnosis would tend to facilitate communication. However, communication may be hampered by the loss of several PDs with which clinicians are familiar (Clarkin & Huprich, 2011). Trait approaches may be unfamiliar to clinicians, who may also find the trait system of the *DSM-5* overly complex (Clarkin & Huprich, 2011). However, trait ratings solve the problem posed by the regular diagnosis of PD NOS (Krueger, Eaton, Derringer, et al., 2011), and over time clinicians will likely become more familiar with the *DSM-5* traits. It is also useful to note that the 25 facets of the *DSM-5* represent a dramatic reduction from the 79 to 99 symptom criteria of *DSM-III* and *DSM-IV* (Krueger, Eaton, Clark, et al., 2011). Finally, although it is clinically important to depict personality-related strengths (e.g., Bornstein, 2011a; Hopwood, 2011), the *DSM-5* provides no mechanism for doing so, as all of the elements of PD diagnosis are pathological.

Overall, the *DSM-5* Section II model has not been particularly useful to clinicians wishing to select effective interventions, as there are no evidence-based interventions for most PDs, and treatments that do exist are only modestly helpful (Matusiewicz et al., 2010). There are reasons to think that the *DSM-5* Section III model could lead to more effective interventions. For instance, the development of treatment methods to differentially target personality pathology or particular types/traits of PD style could enhance the specificity of therapeutic techniques. However, the issue of treatment selection has rarely been discussed in debates about how to classify PDs, suggesting that improvements in this regard attributable to the *DSM-5* Section III are likely to be modest (Clarkin & Huprich, 2011).

The *DSM-5* has perhaps made the most significant progress in terms of helping clinicians differentiate disorder from nondisorder. The quantification of levels provides clinicians with a clear basis for determining a patient's diagnostic standing. Several aspects of the *DSM-5* Section III model may also improve clinical predictions about course and prognosis. Dimensional models of PD are more stable and more valid for predicting prospective outcomes (Morey et al., 2007), suggesting that their incorporation in the *DSM-5* should improve clinical predictions. The separation of levels of functioning from PD styles may improve prognostic predictions if, for

instance, it is shown that personality pathology is more stable than PD instantiations. As discussed earlier, for this reason it is wise that the *DSM-5* is being regarded as a living document that can be modified in order to incorporate new information, such as the stability and long-term predictive validity of different elements of PD diagnosis (Krueger, Eaton, Derringer, et al., 2011).

CASE STUDY

We will demonstrate differences between the *DSM-5* Section II and III models using the case of Elaine, a 28-year-old single, unemployed woman. Elaine presented for an evaluation at a low-fee outpatient clinic unkempt and in clear distress, although her behavior was appropriate and she established rapport readily. The clinician experienced her as thoughtful, warm, and insightful and reported that she had provoked in him a strong desire to be helpful to her. Elaine sought psychotherapy shortly after her life circumstances had worsened considerably. She had been evicted from her apartment 1 month prior and had been living in a homeless shelter. During that time, she had stolen money to buy alcohol and food. She had begun cutting herself on her arms and legs with thumbtacks and broken glass in moments of acute despair, something she had done on a few occasions during dramatic romantic break-ups in adolescence, but that she had discontinued since that time. She denied suicidal intent but acknowledged multiple potentially self-harming behaviors, such as promiscuous sex and careless substance use, in the past and present.

Elaine described being the lone child in an intact, middle-class family as "mostly okay," although she also reported being estranged from her physically abusive father for the 10 years since she had moved out of her parents' house. She maintained a close relationship with her mother, but their contact was somewhat limited due to the ongoing rupture between Elaine and her father. She also had several close friends whom she felt she could trust, although she reported feeling too ashamed to turn to them for help when she really needed it. During adolescence and early adulthood, Elaine had been convicted several times for petty theft. She reported that she had generally stolen or shoplifted with or for her boyfriends in the distant past, but that in the previous few years she had primarily shoplifted alcohol or food for her own consumption. Elaine did well academically and reported many positive social experiences and stable friendships during adolescence, although this time was also colored by several emotionally charged and disruptive romantic breakups. She described several instances in which she behaved in a manner she later regarded as embarrassing in order to attract the attention of a potential suitor. For instance, when Elaine was 16, she shared seductive pictures of herself with a boy that she liked, who then showed the pictures to his friends. When she learned he had done this, she drank heavily, had a sexual liaison with the boy's friend, and threw a rock through his bedroom window. She was charged, convicted, and put on probation, which she later violated; her social reputation also predictably suffered.

Elaine's personality problems were exacerbated 3 years prior to her visit when she witnessed the death of her daughter in an automobile accident. Elaine had been driving, but the accident was not her fault. After being left by her daughter's father shortly after conception, she had cared for her daughter alone and reported that doing so was her main motivation to limit her drinking and work reliably. Following the

accident, Elaine had persistent posttraumatic symptoms, including reexperiencing, avoidance of social events, exaggerated startle, nightmares, and generalized anxiety. She had a history of alcohol abuse that had reached dependence in the past 2 years and had become sufficiently severe to cost her a job 6 months prior to her presentation. She also reported that following the accident, she became disinterested in a committed relationship with a man, although she continued to have multiple sexual relationships.

In terms of personality diagnosis, Elaine has several borderline characteristics with some historical precedent but which had become more severe following her daughter's death. She claimed that every man with whom she had ever had a close romantic relationship had been verbally or physically abusive. She described a host of brief and volatile relationships characterized by a pattern of events involving intense anger over seemingly minor issues, followed by impulsive behavior such as substance abuse or infidelity, and a deep sense of emptiness and regret. She reported feeling so ashamed of herself and angry at her partner following these episodes that she would end relationships rather than acknowledge her behavior or attempt to repair the relationship. Notably, Elaine also reported impulsive, and often attention-seeking, behavior associated with a particularly positive mood. She said that when she felt good, she "just doesn't want it to end," so she "lets it all hang out," which typically involves behaviors such as substance abuse and promiscuous sex that ultimately lead to her feeling lonely and empty.

DSM-IV Diagnosis

From the perspective of the *DSM-5 Section II*, Elaine would meet seven of nine criteria for borderline PD: unstable relationships, identity disturbance, impulsivity, suicidal gestures, affective instability, emptiness, and anger. She would not meet the criteria for dissociative symptoms/paranoid ideation. Although her thinking became somewhat loose during moments of extreme distress, this symptom was not severe enough to be rated as fully present. She also denied abandonment concerns. Elaine would also meet criteria for antisocial PD, having met for adolescent conduct disorder and six of seven antisocial criteria (failure to conform, deceitfulness, impulsivity, irritability, recklessness, irresponsibility) and for histrionic PD, having five of eight symptoms (inappropriate sexuality, rapidly shifting emotions, use of appearance for attention, impressionistic speech, and theatricality). She would, therefore, be well categorized as having prominent Cluster B personality pathology and in particular borderline, antisocial, and histrionic features.

DSM-5 Diagnosis

DSM-5 Section III PD diagnosis occurs in several steps. The first involves rating overall personality pathology. A rating of 3, indicating serious impairment, seemed most appropriate for Elaine in terms of both self- and interpersonal functioning. Her self-system was poorly regulated and unstable, with some boundary definition problems and a fragile self-concept. Her sense of agency was weak, and she commonly felt empty. She often experienced life as meaningless or dangerous. There was sufficient self-functioning that a rating of 4, indicating extreme impairment, did not seem warranted. She was able to regulate her self-states more often than not, and she

was able to articulate a unique identity. There was some evidence of agency and transient fulfillment. Interpersonally, she was able to have stable attachments to individuals outside of romantic relationships, and in these contexts was generally able to understand others' behaviors and motivations empathically. However, she was not able to use these relationships when she needed social support the most, and the negative impacts of her interpersonal dysfunction in romantic relationships were profound.

Elaine did not meet the criteria for any of the PD types, including borderline or antisocial. For borderline, she was missing some criterion A features such as perceptual dysregulation and a desire to avoid abandonment, and she did not have the required criterion B traits of risk taking or hostility (scores on these traits range from 0—not present to 3—present). Most of the criterion A and B features for antisocial were absent. Thus, she would be classified as PD trait specified, with prominent negative affectivity (emotional lability) and disinhibition (recklessness, impulsivity, and irresponsibility).

Is this an improvement? Section III appears to offer a richer description than Section II, in that it quantifies personality pathology, separates personality pathology from PD features, and lists PD features in more detail. Furthermore, the Section II antisocial diagnosis was accurate given her symptoms but did not seem to capture her very well. That said, from a clinical perspective the term borderline does seem to describe Elaine overall, and perhaps more efficiently than the trait-specified diagnosis. The question of optimal models of PD diagnosis cannot be answered using a single study or single case example, and it is likely that there will be strengths and weaknesses of any model of PD. Thus this question will need to be answered by the future researchers and clinicians who use the *DSM-5*.

Table 20.1
Elaine's *DSM-5* Personality Disorder Trait Profile

Negative Affectivity	3
Emotional Lability	3
Anxiousness	2
Submissiveness	1
Separation Insecurity	2
Perseveration	0
Hostility	1
Restricted Affectivity	0
Detachment	1
Social Withdrawal	1
Suspiciousness	2
Depressivity	2
Anhedonia	1
Intimacy Avoidance	0
Antagonism	1
Callousness	0
Manipulativeness	1

Grandiosity	0
Attention Seeking	2
Deceitfulness	1
Disinhibition	3
Impulsivity	3
Distractibility	2
Recklessness	3
Irresponsibility	3
Rigid Perfectionism	0
Risk Taking	0
Psychoticism	1
Unusual Perceptions/Experiences	0
Eccentricity	0
Perceptual Dysregulation	2

SUMMARY

In this chapter, we have described personality pathology and PDs, reviewed their history, clinical presentation, and construct validity, and compared the *DSM-5* Section II and III models of PD with a clinical case. In general, it can be concluded that personality pathology is common and associated with profound functional impairments and personal and societal costs. Although recent research advances provide new, promising methods for assessing and treating PDs, much remains unknown about how to assess and treat personality problems. The upcoming *DSM-5* could contribute to further understanding and clinical utility. However, there is a long history of research and clinical neglect on PDs, so understanding of many aspects of personality pathology is severely limited. Future directions for research include better understanding associations between normative traits and personality-related impairments, developing stronger links between research and practice, and incorporating dynamic elements of personality into existing models. Advances in these areas should contribute to an improved understanding of etiology and ultimately to more effective assessment and treatment methods.

NOTE

1. Kraepelin's conceptualizations also profoundly influenced theories of psychiatric classification in other countries, and the World Health Organization's *International Classification of Diseases* (ICD) PD model significantly parallels that of the *DSM-IV*.

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