CHAPTER 1

Overview of Schizophrenia

As the most well-known person to be afflicted with schizophrenia, John Forbes Nash serves as a natural starting point to a volume on the disorder. Nash was 30 years old when his difficulties became apparent to others. Until then, he may have appeared odd and socially awkward, but he was professionally successful, having recently been offered a full professorship at MIT. However, Nash himself describes experiencing disappointment that his career was not living up to his own expectations (Beck & Nash, 2005). The emergence and profound disruption of Nash's psychotic disorder has been captured by schizophrenia researcher Michael Foster Green (2003):

> His colleagues recall how, in 1959, he walked into a common room at MIT one day and commented that the story on the cover of the *New York Times* contained cryptic messages from inhabitants of another galaxy that only he could decipher. For the next three decades, Nash was in and out of psychiatric hospitals. When he was not in a hospital, he was described as a "sad phantom" who haunted the halls of Princeton "oddly dressed, muttering to himself, writing mysterious messages on blackboards, year after year." (p. 87)

Nash presents a tragic scenario: an eccentric, intellectually brilliant individual beset with extravagant psychiatric symptomatology that wreaks per-

sonal, social, and vocational havoc, leading to decades of cyclical encounters with psychiatric services. Highlighting the link between symptoms and functional disability, Nash's pervasive difficulty in day-to-day living appears rooted in the positive symptoms of schizophrenia (Andreasen, 1984b; Cutting, 2003), which include hallucinations (he hears "voices"[1]), delusions (he believes that the *New York Times* contains special codes sent to him from space), bizarre behavior (he is disheveled and behaves inappropriately), and positive formal thought disorder (his language is difficult to understand). Nash does not appear to have suffered from the negative symptoms of schizophrenia, which include reduced verbal (alogia) and nonverbal expressivity (affective flattening), as well as limited engagement in constructive (avolition), pleasurable (anhedonia), and social (asociality) activity (Andreasen, 1984a; Kirkpatrick, Fenton, Carpenter, & Marder, 2006). Ultimately, Nash's story is one of hope:

> Without warning, Nash started to show signs of recovery in the late 1980s. The reasons for his recovery are still unclear; he was neither taking medications nor seeking help. He started to interact more with mathematicians at Princeton, including several who were old friends. Then in 1994 he won the Nobel Prize in economics. . . . (Green, 2003, p. 87)

In the face of florid symptomatology, behavioral disorganization, and disability, Nash regained much of his lost interpersonal and work-related functioning. Recovery from schizophrenia has been described as an ongoing process of managing symptoms and establishing a sense of purpose (Ralph & Corrigan, 2005); in this respect, Nash certainly has recovered. While Green characterizes Nash's turnaround with the evenhanded caution of a veteran schizophrenia researcher, Nash attributes his own improvement to several factors, the primary cause being acts of reasoning (Beck & Nash, 2005). To illustrate this point, Nash has described, first, convincing himself that the hallucinated voices he was hearing were a product of his own mind, and, later, persuading himself of the improbability and ultimate grandiosity of many of his most cherished beliefs. By adjusting his thinking regarding hallucinations and delusions, Nash diminished symptomatic disruption and brought about considerable improvement in everyday functioning. Nash, thus, exemplifies the cognitive approach to schizophrenia that we advocate in the current volume.

[1]Nash reports that "voices" were a prominent aspect of his experience of schizophrenia beginning in 1959 (Beck & Nash, 2005).

Pioneered in the 1960s (Beck, 1963), cognitive-behavioral models that explain emotional and behavioral responses as products of thoughts, interpretations, and beliefs have proven highly successful in the understanding and treatment of a variety of psychiatric psychopathology—for example, mood disorders, anxiety disorders, substance abuse, and eating disorders (Grant, Young, & DeRubeis, 2005)—as well as somatic pathology—for example chronic pain (Winterowd, Beck, & Gruener, 2003). Furthermore, hundreds of studies now support the basic cognitive model in which beliefs precede and, to a large degree, determine emotional and behavioral reactions (Clark, Beck, & Alford, 1999). Building on preliminary work in the United States (Beck, 1952; Hole, Rush, & Beck, 1979), investigators in the United Kingdom successfully extended the cognitive model into schizophrenia in the 1980s and 1990s (Chadwick, Birchwood, & Trower, 1996; Fowler, Garety, & Kuipers, 1995; Kingdon & Turkington, 2005), producing promising adjunctive psychosocial treatment protocols targeting delusions, hallucinations, and medication compliance (Rector & Beck, 2001).

Cognitive approaches to schizophrenia, of this sort, have certainly advanced the treatment of this very serious condition. We believe that it is important to adapt our knowledge of nonpsychotic conditions to the understanding and treatment of schizophrenia. In a way, the formulation and treatment strategies we advocate are an extension of those that have been successfully applied to depression (Beck, Rush, Shaw, & Emery, 1979), anxiety disorders (Beck, Emery, & Greenberg, 1985), and personality disorders (Beck, Freeman, Davis, & Associates, 2003). However, one size does *not* fit all, and there are important revisions that we must make in the way we approach patients with schizophrenia. Basically, it is crucial to understand the neurocognitive and psychological–cognitive aspect of schizophrenia as well as the uniqueness of schizophrenia as a psychiatric condition. Perhaps there is a continuum in terms of neuropathology and cognitive distortions as we move from the neuroses to the psychoses. But just as water changes character when it goes below the freezing point into ice, so the usual neurotic phenomena do evidence a kind of "deep change" when they become frozen into schizophrenia.

The current volume is intended as an elaboration of the cognitive approach to schizophrenia. We believe that the best psychotherapeutic practice derives from cognitive theory that is grounded in the existing scientific evidence base (Beck, 1976); therefore, the volume is organized into theoretical (Chapters 2–6) and treatment sections (Chapters 7–13), each containing chapters that address the four primary psychopathological dimensions

of the disorder (delusions, hallucinations, thought disorder, and negative symptoms). Additionally, as we also aim to advance the cognitive model of schizophrenia, the final chapter (Chapter 14) presents an integration of the cognitive framework with neurobiological models of schizophrenia. The present chapter provides a brief overview of schizophrenia and our cognitive approach.

BRIEF HISTORY

In this section we focus on the contributions of three pioneers of modern schizophrenia research: John Hughlings Jackson, Emil Kraepelin, and Eugen Bleuler. To a first approximation, Hughlings Jackson's symptom clusters have been superimposed upon Kraepelin's illness category, with causal explanations derived from a Bleulerian cognitive mediational framework. Notably, each theorist grants importance to negative symptoms, despite their differences in defining the disorder.

Hughlings Jackson: Positive–Negative

A highly influential approach to insanity is to be found in the writings of Victorian-era neurologist John Hughlings Jackson (Andreasen & Olsen, 1982; Barnes & Liddle, 1990; Brown & Pluck, 2000). Hughlings Jackson observed (1931):

> Disease is said to "cause" the symptoms of insanity. I submit that disease only produces negative mental symptoms, answering to the dissolution, and that all elaborate positive mental symptoms (illusions, hallucinations, delusions, and extravagant conduct) are the outcome of activity of nervous elements untouched by any pathological process; that they arise during activity on the lower level of evolution remaining. (as cited in Andreasen, 1990b, p. 3)

Composed in the 1880s, Hughlings Jackson's formulation succinctly sums up the theoretical framework that still guides most schizophrenia research (Andreasen, Arndt, Alliger, Miller, & Flaum, 1995; Meares, 1999). At least three points bear mention. First, Hughlings Jackson classifies insanity as a brain disease that is caused by a particular pathology localized in highly evolved (i.e., cortical) neurological centers. Second, he codifies the mad-

deningly varying symptomatology of insanity into a bicameral and heuristic framework vis-à-vis normality. Elaborations and distortions of normal perception, belief, and behavior are brought together under the umbrella term *positive mental symptoms*; these symptoms are embellishments of normal experience. Likewise, deficits in speech, motivation, emotion, and pleasure are grouped as *negative mental symptoms*; these symptoms represent losses relative to normal experience. Third, and perhaps most important, Hughlings Jackson proposes an intuitive causal interface of biology and manifest symptomatology: Negative symptoms are deficit states and naturally suggest underlying, disease-compromised brain structures (i.e., neuropathology); positive symptoms are elaborations on what is normal and naturally suggest an underlying cognitive process (i.e., failure of inhibition). Although Hughlings Jackson didn't speculate regarding prognosis and outcome of insane patients, it might be inferred that the "broken brain" disease process he postulated for negative symptoms might augur particularly unfavorably.

Crow's (1980) highly influential type I/type II model of schizophrenia, which is essentially a modern elaboration of Hughlings Jackson's framework, sparked renewed interest in the negative symptoms of schizophrenia (Morrison, Renton, Dunn, Williams, & Bentall, 2004). Compelled by new findings in the neurobiology of schizophrenia emerging at the time, Crow proposed splitting schizophrenia into two distinct disorders. Individuals collected under type I schizophrenia manifest marked positive symptoms, respond well to psychoactive medication, and have an illness course characterized by sudden onset and favorable long-term outcome. Individuals grouped as having type II schizophrenia, by contrast, manifest predominantly negative symptomatology, do not respond well to medications, and have an illness course characterized by insidious onset and poor long-term outcome. Crow argued, further, that neurochemical imbalance related to the neurostransmitter dopamine underlies type I schizophrenia, whereas structural brain abnormality such as reduced cerebral volume underlies type II schizophrenia.

The impact of Crow's model has been considerable (Bentall, 2004), as the Hughlings Jackson-inspired conceptual parameterization of positive and negative symptom groupings has come to dominate schizophrenia theory and research (Healy, 2002). Of primary importance, investigators developed operationalized rating scales focused upon the positive and negative symptoms of schizophrenia—for example, the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984c), the Scale for the Assess-

ment of Negative Symptoms (SANS; Andreasen, 1984b), and the Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein, & Opler, 1987). Andreasen's scales (i.e., SAPS and SANS), in particular, are comprehensive, standardized instruments, in which a sizeable array of symptoms is identified in observable terms (see Chapter 7). Psychometrically, these scales have been shown to be reliable and sensitive to change (Andreasen, 1990a).[2]

Kraepelin's Heterogeneous Category

Whereas Hughlings Jackson produced a framework that guides brain–behavior theory and research, it is the German psychiatrist Emil Kraepelin who devised the modern classificatory system, or nosology, for schizophrenia (Healy, 2002; Wing & Agrawal, 2003). Based upon extensive patient observation, Kraepelin (1971) collected three diverse manifestations of insanity—hebephrenia (aimless, disorganized, and incongruous behavior), catatonia (lack of movement and stupor, on the one hand; agitated, incoherent behavior, on the other), and paranoia (delusions of persecution and grandeur)—and placed them into a single disease category that he termed *dementia praecox*. Characteristic symptoms included some that Hughlings Jackson would have termed positive (i.e., hallucinations, disorganized speech, and delusions). However, dementia praecox was ultimately a deficit state, making symptoms Hughlings Jackson might have termed negative central to the condition, that is, "emotional dullness, failure of mental activities, loss of mastery over volition, of endeavor, and ability for independent action" (as cited in Fuller, Schultz, & Andreasen, 2003, p. 25).

It is this fundamental illness chronicity combined with a progressively degenerative course that lead Kraepelin to categorize *dementia praecox* distinct from cyclical, mood-related psychotic conditions such as mania and melancholia, which he aggregated into a second disease category, manic–depressive psychosis. Course and long-term outcome, in this manner, guided Kraepelin's nosological efforts more than manifest symptomatology (Healy, 2002). Although he believed that patients could recover from manic–depression, Kraepelin was deeply pessimistic regarding recovery from dementia praecox (Calabrese & Corrigan, 2005; Warner, 2004).

[2]We note that there is debate regarding the limitations of the SAPS and SANS to capture the symptoms of schizophrenia (e.g., Horan, Kring, & Blanchard, 2006).

Though the term dementia praecox has fallen out of favor, Kraepelin's category is very much evident in the diagnostic criteria of two influential codifications of mental disorders: the American Psychiatric Association's (2000) *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV-TR) and the World Health Organization's (1993) *International Classification of Diseases*, 10th revision (ICD-10). According to both the DSM-IV-TR and ICD-10 (see Table 1.1), there are five characteristic symptoms of schizophrenia: delusions, hallucinations, disorganized speech (e.g., frequent derailment or incoherence), grossly disorganized or catatonic behavior, and negative symptoms (i.e., affective flattening, alogia, or avolition) (Wing & Agrawal, 2003). The two systems do differ on a few points, such as the amount of time the symptoms need to be expressed to reach criterion (DSM-IV > ICD-10), as well as whether functional disturbance is intrinsic to the diagnosis of schizophrenia (DSM-IV = "yes"; ICD-10 = "no").

However, heterogeneity is built into the definition of schizophrenia: at most, two of the five symptom types need be present to qualify for diagnosis, and under specified conditions of severity (e.g., two voices comment-

TABLE 1.1. Diagnosis of Schizophrenia

Symptoms	Two symptoms present for at least 1 month: (positive) delusions, hallucinations, disorganized speech, disorganized or catatonic behavior; (negative) affective flattening, alogia, avolition.
Social dysfunction	One or more areas affected for most of the time since onset (required by DSM-IV): work, interpersonal relations, self-care; if during adolescence, failure to reach level of interpersonal, academic, or occupational achievement.
Duration	Active symptoms of psychosis must persist in absence of treatment: ICD-10 active symptoms for at least 1 month; DSM-IV active symptoms for at least 6 months, including prodromal and residual (negative or attenuated positive) symptoms.
Exclusion of other disorders	Other diagnoses with psychiatric symptoms must be excluded: schizoaffective disorder; major depression with psychosis; substance abuse disorders; medical disorders such as head injury, cerebral vasculitis, stroke, and dementia.

Note. Adapted from Schultz and Andreasen (1999). Copyright 1999 by Elsevier. Adapted by permission.

ing on behavior), just one symptom needs to be present. The end result is the possibility that two patients who share the diagnosis of schizophrenia might not share any common symptoms. Yet, this heterogeneity of the concept of schizophrenia is by design, as it follows from Kraepelin's assembly of a mental disease category from syndromes characterized by diverse symptomatology (Bentall, 2004; Healy, 2002). Thus, the five-choose-two scheme allows both the DSM-IV and the ICD-10 to include Kraepelin's paranoid, catatonic, and hebephrenic (in DSM-IV, disorganized) subtypes, because diagnosis of each type requires no more than two of the five symptoms of schizophrenia. Additionally, both the current DSM-IV and ICD-10 classifications follow Kraepelin in categorizing schizophrenia separately from affective psychoses (e.g., bipolar disorder).

The inherent heterogeneity of the category *schizophrenia* complicates research efforts, as it naturally leads to conflicting findings. Some researchers have responded to this problem by attempting to define more homogeneous subcategories of schizophrenia (e.g., Carpenter, Heinrichs, & Wagman, 1988), whereas others have abandoned the categorical illness model in place of a disorder defined in terms of severity on a discrete set of symptom dimensions (van Os & Verdoux, 2003). However, difficulty with DSM-IV, and therefore Kraepelinian, classification is not confined to heterogeneity. Critics (Healey, 2002) have observed that the DSM scheme has unsatisfactory reliability, and that the subcategories are not temporally exclusive (i.e., different subtypes can apply to the same patient at different points in time). Further, the symptoms of schizophrenia are not diagnostic or pathognomic. That is, delusions and hallucinations can be found in a variety of neurological and psychological conditions (Wong & Van Tol, 2003), as can disorganized and negative symptoms (Brown & Pluck, 2000). Finally, despite hundreds of studies locating physiological correlates of schizophrenia, no biological marker has been discovered that distinguishes the physiology of someone diagnosed with a psychotic disturbance from normal physiology (Wing & Agrawal, 2003; Wong & Van Tol, 2003). Indeed, Heinrich's (2005) recent quantitative review of biological studies finds considerable overlap between schizophrenia and control samples (see Chapter 2).

Bleuler's Cognitivism

The Swiss psychiatrist Eugen Bleuler (1911/1950) is schizophrenia's other founding father, and, indeed, he is credited with coining the term *schizophrenia* itself. More important, he characterized schizophrenia as a family

of mental disorders (Healy, 2002) and thereby expanded the frontiers of inclusion considerably beyond Kraepelin's formulation. Bleuler's formulation was essentially dimensional (Wing & Agrawal, 2003), as it spanned from mild personality dysfunction of the kind that would later be termed schizotypy/schizotaxia to full-blown, chronic *dementia praecox*. Bleuler's model of psychopathology, like that of Hughlings Jackson, characterized the disturbance of schizophrenia in terms of primary (fundamental) and secondary (accessory) symptoms. Primary symptoms—which were necessary for diagnosis, present in every case, and caused by the basic neuropathology—included loss of continuity of associations, loss of affective responsiveness, loss of attention, loss of volition, ambivalence, and autism (Fuller et al., 2003). Secondary symptoms—which did not have to be present for diagnosis and were not caused by the underlying neuropathology—included hallucinations, delusions, catatonia, and behavioral problems (Warner, 2004; Wing & Agrawal, 2003). Quite importantly, from a theoretical standpoint, Bleuler proposed that a cognitive process—loosening of associations—played an intermediary or mediational role between the obscure neuropathology and the expression of symptoms and signs characteristic of schizophrenia. Indeed, it is this very loosening of associations that the term *schizophrenia* (i.e., *schizo* = to split; *phrene* = mind) is designed to capture.

Bleuler's impact upon schizophrenia research is considerable. First, he widened the concept to include what would later be called schizotypal and schizoid traits that are currently included as personality disorders in the DSM-IV. Much genetic, neurobiological, and diagnostic research, moreover, has been devoted to this "schizophrenia spectrum" over the past 40 years (O'Flynn, Gruzelier, Bergman, & Siever, 2003). More important, arguably, is Bleuler's conceptualization of the mechanics of the disorder; he postulated an intermediary cognitive process that links the as-yet unclear neuropathology to manifest symptoms of the disorder (Bentall, 2004). Theorists of all stripes claim this Bleulerian mantle. Thus, neuropsychological (Andreasen, 1999; e.g., Frith, 1992; Green, Kern, Braff, & Mintz, 2000), psychodynamic (e.g., McGlashan, Heinssen, & Fenton, 1990), and cognitive-behavioral (e.g., Kingdon & Turkington, 2005) theorists all work within a Bleulerian framework. Our theoretical approach is also Bleulerian (see Chapters 3–6). Indeed, Chapter 14 presents a new model of schizophrenia that integrates developmental, biological, cognitive, and psychological findings within a mediational framework that both motivates the rationale for psychosocial intervention and identifies specific therapeutic targets.

WHAT WE KNOW AND DON'T KNOW ABOUT SCHIZOPHRENIA[3]

It has now been nearly 100 years since Kraepelin and Bleuler originated the modern concept of schizophrenia, and an enormous amount of research has accrued over this time period, especially in the last 25 years. In 1988, the lead article in the inaugural issue of *Schizophrenia Research* was titled, "Schizophrenia, Just the Facts: What Do We Know, How Well Do We Know It?" (Wyatt, Alexander, Egan, & Kirch, 1988)." The literature on schizophrenia has become too vast and unwieldy to tightly summarize in the manner of Wyatt et al.; nonetheless, we intend the current section as a thumbnail sketch of the current state of knowledge about schizophrenia.

Characteristic Symptom Dimensions

As we have seen, schizophrenia has a diverse symptom presentation, and an important research program has been to determine if the symptoms tend to cluster in a particular manner. If, say, hallucinations and delusions tend to co-occur, this might suggest a common, underlying neurobiological pathology. A consensus has now emerged, based upon factor-analytic studies conducted in several cultures, that, at minimum, three dimensions account for the symptoms of schizophrenia (Andreasen et al., 1995, 2005; Barnes & Liddle, 1990; Fuller et al., 2003; John, Khanna, Thennarasu, & Reddy, 2003): (1) psychotic symptoms (hallucinations and delusions), (2) disorganized symptoms (bizarre behavior and positive formal thought disorder), and (3) negative symptoms (flat affect, alogia, avolition, and anhedonia). This consensus has lead to a validation of the specific symptom dimensions (Earnst & Kring, 1997) and, correspondingly, has paved the way for the formulation of symptom remission criteria for schizophrenia (Andreasen et al., 2005). Carpenter (2006) has observed that the emerging database on symptom clusters has helped to return the schizophrenia concept to its Kraepelinian and Bleulerian roots, because it corrects the overly narrow definition of schizophrenia as predominantly a psychotic disorder that has enjoyed prominence in psychiatry over the past 40 years.

[3]Angus MacDonald and the Minnesota Consensus group are compiling a more complete list of facts about schizophrenia that is to be published in the March 2009 issue of *Schizophrenia Bulletin*. The title of the section has been adapted from their working report, which appeared on the *Schizophrenia Research Forum* website (*www.schizophreniaforum.org/whatweknow/*) in mid-2007.

Epidemiology

As John McGrath (2005) has observed, epidemiology in schizophrenia has undergone a mini-revolution in the past decade. The view that schizophrenia is a catholic illness that inexorably affects 1 in 100 persons regardless of gender (Buchanan & Carpenter, 2005; Crow, 2007) is giving way to a more nuanced perspective. Schizophrenia appears to have a .7% prevalence rate that varies considerably across cultures (a five-fold difference). Men are at greater risk than women to develop the disorder and tend to develop the disorder earlier. The incidence of new cases of schizophrenia is .03% and may be declining (McGrath et al., 2004). Incidence also varies across culture. Being born or residing in an urban setting is associated with greater risk for developing schizophrenia (Mortensen et al., 1999). Migrants, additionally, have an increased risk of developing schizophrenia; this is especially true if the migrants have dark skin and migrate to an area with a light-skin dominant group (Boydell & Murray, 2003). African Americans are 3 times more likely to develop schizophrenia than European Americans (Bresnahan et al., 2007). Schizophrenia is also associated with increased mortality. Individuals with schizophrenia die prematurely (Brown, 1997). Suicide is a major contributor to this discrepancy, and it has been estimated that 5.6% of individuals diagnosed with schizophrenia die by suicide, with the period of greatest risk coming during the early phase of the illness (Palmer, Pankratz, & Bostwick, 2005). While individuals with schizophrenia are 13 times more likely to die by suicide than individuals in the general population, Saha and colleagues (Saha, Chant, & McGrath, 2007) have recently shown that individuals with schizophrenia also have elevated mortality across a wide array of illness categories.

Genetic and Environmental Risk Factors

Genetics

Eighty years of behavior genetics research in the form of twin, family, and adoption studies indicate that schizophrenia is highly heritable. Family studies have consistently shown that schizophrenia runs in families and that the degree of genetic sharing with the affected member predicts the likelihood of developing schizophrenia (Nicol & Gottesman, 1983). A recent quantitative review of 11 well-conducted family studies found that first-degree relatives of persons with schizophrenia are 10 times more likely to develop schizophrenia than nonpsychiatric comparison subjects (Sullivan, Owen, O'Donovan, & Freedman, 2006). Adoption studies provide

more support for the contribution of genetic factors to the development of schizophrenia. A quantitative review found no difference in the rates of schizophrenia in the adoptive relatives of individuals with and without schizophrenia; however, biological relatives of adoptees with schizophrenia are 5 times more likely to develop schizophrenia than the biological relatives of adoptees who do not have schizophrenia (Sullivan et al., 2006). In other words, there is little evidence in these studies to support the role of post-adoption environmental factors in the etiology of schizophrenia, which stands in contrast to the evidence for genetic influence. In identical twin pairs, if one twin has schizophrenia, the other twin has nearly a 50% chance of also developing schizophrenia (Cardno & Gottesman, 2000). Such high rates of concordance have led many to observe that a great proportion of the liability for schizophrenia is genetic (Gottesman & Gould, 2003; Riley & Kendler, 2005). Indeed, Sullivan, Kendler, and Neal (2003), in a quantitative review of 12 twin studies, propose a heritability estimate of 81% for genetic factors in the liability of developing schizophrenia. In other words, four-fifths of the variability in schizophrenia liability is due to additive genetic effects.

Although behavior genetics research has established the importance of genes in the development of schizophrenia, specific genes and the mechanistic details remain unclear. With the exception of Crow (2007), who believes that schizophrenia is conferred by a single gene related to language that is to be found on the sex chromosome, the field of schizophrenia genetics now embraces the conclusion that many susceptibility genes contribute to schizophrenia, each gene having but a small effect in the overall etiology of the disorder (Gottesman & Gould, 2003; Sullivan et al., 2006). Thus far, a dizzying array of candidate genes has been identified (Sullivan et al., 2006). Owen, Craddock, and O'Donovan (2005) propose that case-control variations in a few of the candidate genes (e.g., neuroregulin 1 and dystrobervin binding protein 1) have been replicated several times, making these genes the most likely schizophrenia genes at the present (see Chapter 2). These best candidate genes, further, are present in a fraction of patients with schizophrenia (between 6 and 15%) and increase the liability by at most a factor of two (Gilmore & Murray, 2006).

Environment

While lack of perfect concordance between identical twins has been taken as evidence for the role of nongenetic factors in the etiology of schizo-

phrenia, Sullivan et al. (2003), in their quantitative review of twin studies, express considerable surprise that the analysis also reveals a significant effect (a heritability estimate of 11%) for nonshared environment in the etiology of schizophrenia. There is now considerable evidence implicating environmental factors in the etiology of schizophrenia. Mary Cannon and colleagues (2002), for example, have conducted a quantitative review that identified three groupings of obstetric complication associated with schizophrenia: complications occurring during pregnancy (e.g., bleeding, diabetes), complications occurring at the time of delivery (emergency cesarean delivery, asphyxia), and abnormal fetal growth and development (e.g., low birth weight). The risk of schizophrenia associated with obstetric complications is double that without such complications, a small effect that is comparable in magnitude to the risk associated with variation in particular genes (Gilmore & Murray, 2006). The second trimester of pregnancy is particularly key for neurodevelopment, and there is evidence that insults at this phase of development (e.g., the mother acquiring an infection or being unduly stressed) approximately double the risk of offspring developing schizophrenia (Cannon, Kendell, Susser, & Jones, 2003) .

Environmental factors that occur considerably after birth have also been implicated. As we have seen, schizophrenia is disproportionately represented in urban environments (McGrath et al., 2004). Because urban inhabitance and birth are highly correlated, it is not clear whether the observed elevations are due to prenatal or perinatal factors associated with an urban birth, or whether urbanicity confers risk at a later point in development in the form of psychosocial stress and social isolation (Boydell & Murray, 2003). In this regard, a recent prospective study involving more than 300,000 Israeli adolescents is notable, as the researchers found an interaction between population density and factors related to the genetic risk for schizophrenia (poor social and cognitive functioning), suggesting that the stress of city living might combine with genetic vulnerability to produce schizophrenia (Weiser et al., 2007). In a similar fashion, a recent quantitative review of seven studies estimates that cannabis use during adolescence increases the risk of the subsequent development of psychosis by two to three times (Henquet, Murray, Linszen, & van Os, 2005). Further, there is evidence of a gene–environment interaction, as individuals who have a variant of the catechol-*O*-methyltransferase (*COMT*) gene, roughly 25% of the population, are the ones who show elevated risk associated with adolescent cannabis consumption (Caspi et al., 2005). *COMT* is not, importantly, associated with elevated cannabis consumption.

Neurobiological Factors

As we have seen, it has been apparent in psychiatry since the mid-19th century that the behavioral, emotional, and cognitive features of schizophrenia ought to be rooted in the brains of affected individuals (Hughlings Jackson, 1931), a position that has been strengthened by the development of effective antipsychotic medications (Healy, 2002). Brain malfunction or abnormality (termed "pathophysiology") could be responsible for schizophrenia in either of two basic ways: (1) the structure of the brains of individuals with schizophrenia could differ from normal (anatomical pathology), or (2) the functional activity of the brains of individuals with schizophrenia could differ from normal (physiological pathology). As simple and obvious as this formulation might appear, 100 years of schizophrenia research has yet to produce a coherent and agreed-upon account of necessary and sufficient neurobiological factors and processes that distinguish individuals with schizophrenia from individuals who do not develop the disorder (Williamson, 2006). In other words, the pathophysiology of schizophrenia remains elusive (see Chapter 2).

Anatomical Abnormality

Nonetheless, considerable advances have been made in the understanding of the neurobiology of schizophrenia. One approach has been to investigate the anatomy of brains of individuals with schizophrenia after they have died. Postmortem research of this sort has produced two important conclusions: (1) Schizophrenia is not a neurodegenerative illness in the manner that Kraepelin (1971) and his followers supposed, and (2) patients with schizophrenia show evidence of abnormal cellular architecture as compared to the brains of healthy controls. As an example of this latter effect, David Lewis and his colleagues have shown in several studies that, relative to controls, individuals with schizophrenia evidence reduced densities in the input layers of pyramidal cells within the dorsolateral prefrontal cortex (Lewis, Glantz, Pierri, & Sweet, 2003).

Structural imaging has been another fruitful avenue for discovering anatomical differences associated with schizophrenia. Indeed, the oldest image of the living brain of an individual diagnosed with schizophrenia is remarkable, not only because the patient endured the replacement of her cerebrospinal fluid with air, but because the enlargement of the lateral ventricles is visible (Moore, Nathan, Elliott, & Laubach, 1935). Larger ventricles are associated with more cerebrospinal fluid and smaller brain size,

and subsequent imaging studies found evidence that ventricular enlargement is a general feature of schizophrenia (Johnstone & Ownes, 2004; Vita et al., 2000). In a systematic review of 40 studies, Lawrie and Abukmeil (1998) estimated a 30–40% median increase of lateral ventricle volume when patients with schizophrenia are compared to controls, as well as a median reduction in overall brain volume of 3%. In a quantitative review of 155 structural imaging studies, Davidson and Heinrichs (2003) report that frontal and temporal structures, especially the hippocampus, tend to be smaller in patients with schizophrenia relative to healthy controls. More recent reviews have established that volumetric abnormality is present at the outset in schizophrenia, as first episode patients already have larger ventricles, reduced brain volume, and reduced hippocampal volume, compared to matched controls (Steen, Mull, McClure, Hamer, & Lieberman, 2006; Vita, De Peri, Silenzi, & Dieci, 2006). Indeed, unaffected relatives also appear to have ventricalur enlargement and hippocampal reduction relative to control individuals (Boos, Aleman, Cahn, Hulshoff Pol, & Kahn, 2007), suggesting that anatomical differences might be related to the genetic vulnerability for schizophrenia. However, all observed structural differences are relatively small (0.5 *SD* between patients and controls, 0.33 *SD* between first-episode patients and controls, one-fifth an *SD* between unaffected relatives and controls), sharing considerable overlap with healthy samples (Heinrichs, 2005). The results of a recent imaging study are consistent with the conclusion that a complex set of small differences across the entire cortex characterizes the difference between individuals with schizophrenia and normal controls (Davatzikos et al., 2005).

Functional Abnormality

Having patients engage in a task while measuring regional brain activation is a promising means of determining physiological differences associated with schizophrenia. Early studies, utilizing positron emission tomography (PET), evidenced abnormal activation patterns across many regions of the brain in response to a task (Gur & Gur, 2005). Quantitative review of this literature suggests that the strongest difference is a lack of task-related activation of the frontal lobes (so-called hypofrontality) in individuals with schizophrenia as compared to healthy controls (Davidson & Heinrichs, 2003). More fine-scaled analysis of 12 studies suggests that the brain-activation pattern during working memory tasks is more complex than the hypofrontality hypothesis might lead one to believe, involving both hypoactivation and hyperactivation of a variety of structures (Glahn

et al., 2005). Many other differences in task-related activation have been identified (Belger & Dichter, 2005; Gur & Gur, 2005) across a variety of cognitive, behavioral, and emotion-based tasks. Most of the differences are small, many not replicated—factors that inhibit generalized conclusions regarding functional differences in schizophrenia (see Chapter 2).

Neurocognitive Factors

Both Kraepelin and Bleuler observed difficulties in schizophrenic patients' cognitive processes of attention, memory, and problem solving, and systematic tests were developed by the 1940s; however, much of what is known regarding the cognitive impairment in schizophrenia has accrued since a concerted research effort began in the 1980s (Goldberg, David, & Gold, 2003). Reichenberg and Harvey (2007) report a review of quantitative reviews from 12 domains, including general intellectual ability, verbal memory, nonverbal memory, recognition, executive functions, motor skills, working memory, language, attention, and processing speed. The main finding, consistent with the older reports, is that patients perform more poorly than healthy controls across *all* 12 of the neurocognitive domains, the patient–control difference averaging between a 0.5- and 1.5-standard-deviation shift. In a much cited quantitative review of 204 studies, Heinrichs and Zakzanis (1998) found that patient performance is inferior across all cognitive domains, by nearly a standard deviation on average. There was much variability across tasks, with verbal memory showing the largest difference (nearly 1.5 *SD* shift in the average patient mean relative to the control mean across studies). Heinrichs (2005) has observed that the patient–control differences on neurocognitive tasks are much larger than differences found for neurobiological factors, such as those measured in structural imaging studies. However, there is still a fair amount of overlap between the two groups, leading to the possibility that a proportion of patients is neuropsychologically normal (Palmer et al., 1997)—a position that has not gone unchallenged (Wilk et al., 2005).

Nonetheless, the large patient–control differences have led several authors to refer to cognitive impairment as a central feature of schizophrenia, as well as an important key to understanding its pathophysiology (Gur & Gur, 2005; Heinrichs, 2005; Keefe & Eesley, 2006; MacDonald & Carter, 2002; Marder & Fenton, 2004). Cognitive impairment, indeed, emerges prior to the onset of the first psychosis. Longitudinal studies provide the best evidence. For example, poorer test scores in childhood have been found to predict the development of adult schizophrenia in an English

sample (Jones, Rodgers, Murray, & Marmot, 1994). Similarly, lower test scores on IQ subtests in adolescence predicted the later development of schizophrenia in Swedish (David, Malmberg, Brandt, Allebeck, & Lewis, 1997) and Israeli (Davidson et al., 1999) conscripts. In this later study, the intellectual decline was shown to start during childhood and continue through adolescence and to be independent of gender, socioeconomic status, and the occurrence of nonpsychotic psychiatric disorders (Reichenberg et al., 2005).

These same researchers readministered the IQ subtests to the 44 individuals who developed schizophrenia and found that, though a few tests showed a decline in performance, there was little change on a majority of the tests, suggesting that a substantial proportion of the intellectual decline occurred prior to the onset of the first psychosis (Caspi et al., 2003). And, it appears that the severity of the cognitive impairment in first-episode schizophrenia is indistinguishable (i.e., on the order of an *SD* shift, on average, in performance) from the impairment seen in individuals with chronic schizophrenia (Gold & Green, 2005; Keefe & Eesley, 2006), suggesting that neurocognitive deficiency is one of the stabler aspects of schizophrenia. Adding to this perspective, quantitative reviews suggest that cognitive impairment is one of the best predictors of the poor social and vocational outcomes that are characteristic of a vast majority of individuals with schizophrenia (Green, 1996; Green et al., 2000).

An interesting development in the understanding of neurocognition in schizophrenia is the well-replicated finding that genetic relatives of individuals with schizophrenia show an attenuated cognitive impairment that is more severe than healthy controls (Reichenberg & Harvey, 2007). On average, unaffected relatives differ from controls between 0.2 to 0.5 a standard deviation across domains. Raquel and Ruben Gur and their colleagues have reproduced this same pattern of data in a multigenerational family study, demonstrating that neurocognitive domains may be genetic markers for schizophrenia (Gur et al., 2007).

Treatment and Outcome

As seen in the previous section, the modern image of schizophrenia is that of a complex syndrome caused by a variety of genetic and environmental factors, each making a small contribution to the development of a disorder that entails three basic symptom dimensions, pervasive neurocognitive impairment, and many small neuroanatomical and neurophysiological deficits. The present section addresses one of the great revolutions of modern

psychiatry—the advent of antipsychotic treatment, which couples naturally with a discussion of short- and long-term outcomes achieved by individuals with schizophrenia.

Antipsychotic Medications

It seems hard to believe that antipsychotic medications have been around for just one-half of a century. One of us (Beck) recalls rather vividly a residency rotation in a psychiatric hospital in which patients with schizophrenia were treated with hydrotherapy (some of them drowned) and insulin coma therapy (some of them died). Other patients, quite famously Tennessee Williams's sister, were given frontal lobotomies, a treatment that created as many problems as it solved. In Paris in 1952, Denker and Delay found, quite by accident, that chlorpromazine (brand name Thorazine), the first neuroleptic medication, reduced hallucinations and delusions (Healy, 2002), a finding that would ultimately transform the treatment of schizophrenia, leading to the elimination of the dubious somatic therapeutic regimes that had dominated the treatment of the disorder since the turn of the 20th century. Chlorpromazine was introduced in the United States in 1954, and many sister compounds (family name *phenothiazine*) were soon synthesized and introduced, including haloperidol (Haldol) and perphenazine (Trilafon). With the vast majority of individuals with schizophrenia in the developed world currently taking antipsychotic drugs, it can be hard to appreciate the skepticism that first greeted the reports of the efficacy of neuroleptic medications. However, by the early 1960s, two facts had emerged. First, the National Institute of Mental Health (NIMH) sponsored a collaborative randomized control trial that demonstrated the efficacy of antipsychotic drugs to reduce psychotic symptoms in patients with acute schizophrenia (Guttmacher, 1964). Second, researchers had determined that the mechanism of action of neuroleptic medications was a blockade of postsynaptic receptors of the neurotransmitter dopamine (Healy, 2002; Miyamoto, Stroup, Duncan, Aoba, & Lieberman, 2003). But neuroleptic drugs are "dirty" in that they also affect other neurotransmitter systems in the brain, causing side effects such as sedation, weight gain, and extrapyramidal side effects (see Chapters 2 and 13 for more detail regarding pharmacodynamics of antipsychotic medicines).

Since the mid-1970s, evidence has accrued that antipsychotic medications help to prevent relapses: Patients who discontinue medication are three to five times as likely to relapse as patients who do not discontinue medication; patients switched to placebo show an elevated relapse rate as compared to patients maintained on antipsychotic medication (Marder &

Wirshing, 2003; Stroup, Kraus, & Marder, 2006). The introduction of clozaril (Clozapine) in the 1980s kicked off the second-generation of antipsychotic medication (Healy, 2002). These agents, which include risperidone (Risperdal) and olanzapine (Zyprexa), are the most prescribed medicines for schizophrenia in the United States and Europe, and currently dominate the treatment of the disorder. Second-generation drugs have a different mechanism of action (they antagonize serotonin in addition to dopamine) and were touted as a breakthrough in terms of efficacy (better), side-effect profile (more favorable), and cognitive impairment (reduced) (Healy, 2002). However, research findings have been disappointing in this regard, as well-conducted studies have shown little difference in efficacy between first- and second-generation antipsychotic medications (Lieberman et al., 2005). Neither have the drugs been found to have a better effect on neurocognition (Keefe et al., 2007), leading some researchers to question the greater cost of the newer medicines, especially given the elevated risk for metabolic side effects such as diabetes (Rosenheck et al., 2006). Harrow and Jobe (2007) have recently reported on the result of a 15-year prospective study in which they identify a subgroup of individuals with schizophrenia who discontinue antipsychotic medication and experience periods of recovery. The authors propose that their results suggest that there is subgroup of individuals with schizophrenia who do not need to remain continuously medicated in order to achieve a good outcome.

Outcome

Disagreement regarding prognosis in schizophrenia can, like much else, be traced to Bleuler and Kraepelin. As we have already seen, Kraepelin was deeply pessimistic about the possibility of significant improvement, let alone recovery (Kraepelin, 1971). Indeed, Kraepelin argued that any patient manifesting the symptoms of dementia praecox who subsequently improved must have been misdiagnosed originally (Rund, 1990). Bleuler (1911/1950), by contrast, observed that a majority of his patients improved enough to maintain employment and self-sufficiency. Warner (2004) has suggested that Bleuler's more optimistic perspective on outcome in schizophrenia may have resulted from his superior treatment model, as well as the more favorable economic conditions characteristic of Switzerland at that time.

Calabrese and Corrigan (2005) observe that, in addition to the profound impact of his nosological work, Kraepelin's pessimistic view of outcome in schizophrenia has had a long-term impact upon psychiatry, particularly in terms of treatment expectations. As we have seen, research has

failed to support Kraepelin's central claim that *dementia praecox* is neurodegenerative; however, evidence is more equivocal regarding rates of recovery. Kraepelinian pessimism has tended to prevail within American psychiatry, in particular. Thus, when discussing outcome in schizophrenia, the authors of the DSM-III (American Psychiatric Association, 1980), echoing the pioneer, caution that "remission of symptoms or return to premorbid functioning is so rare that it would likely result in the clinician questioning the original diagnosis" (p. 64). The DSM-IV-TR (American Psychiatric Association, 2000) is not much more encouraging on the subject of outcome in schizophrenia: "Complete remission (i.e., a return to full premorbid functioning) is probably not common in this disorder" (p. 309).

There is some disagreement as to whether the introduction of antipsychotic medication has improved the outcomes achieved by individuals with schizophrenia. Hegarty and colleagues (Hegarty, Baldessarini, Tohen, Waternaux, & Oepen, 1994) report results from a meta-analysis showing that the proportion of good outcomes improved between 1950 and 1980, a period in which the medications became readily available, as compared to 1930–1950. Warner (2004) and others (e.g., Healy, 2002; Peuskens, 2002) have argued, conversely, based upon reviews of the outcome literature, that functional outcomes have not changed dramatically since the introduction of antipsychotics. Either way, a large proportion of patients continue to experience poor long-term outcomes. Hafner and an der Heiden (2003) estimate that the proportion of first-episode patients who demonstrate symptom improvement and have no relapses over 5 years varies from 21 to 30%, suggesting that the majority of patients experience recurrence or continual symptomatology. Hegarty et al.'s (1994) meta-analysis estimated that a clear majority of patients across studies achieve "unfavorable" or "chronic" outcomes. Robinson et al. (2004), in perhaps the best study of this kind, found that 50% of their first-episode patients achieved 2 years of symptom remission (no more than "mild" positive symptoms, as well as no more than "moderate" negative symptoms) over a 5-year follow-up period, while 25% achieved 2 years of adequate social and vocational functioning, and, importantly, just 12% met full recovery criteria for 2 years or more. Given the high quality of treatment delivery and compliance in this study, the result is a sobering portrait regarding the efficacy of existing medication and ancillary treatments to improve social and vocational functioning.

Calabrese and Corrigan (2005) report on the 10 published studies of the long-term course of schizophrenia in which the average time to follow-up assessment was 15 years or more. While these studies differ in terms of the nationality of participants (e.g., German, Japanese, Swiss, American), the definition of schizophrenia (i.e., wide or narrow), the definition

of recovery/improvement (e.g., symptom-based or functioning-based), and the time to follow-up (the average follow-up assessment in this group of studies is 27 years, and the range is 15–37 years), the findings appear to be relatively consistent: That is, roughly 50% of the patients are classified as "recovered or improved." Correspondingly, roughly half of the patients were "not improved or chronic," meaning that, on average, this set of patients experience more than two and a half decades of disability. The World Health Organization International Study of Schizophrenia (Harrison et al., 2001) illustrates this point poignantly. Involving 18 international research centers and 1,633 patients with a psychotic illness, the authors report that outcomes were favorable for more than 50% of the sample followed up. However, this conclusion is based upon a clinical rating made on a 4-point scale, and Harrison et al. (2001) argue that more restrictive definitions of favorable outcome that include explicit functioning requirements are more meaningful. When they set a minimal functioning cutoff (i.e., Global Assessment of Functioning rated 60 or above, indicating "mild, minimal or no difficulty in social functioning"), the percentage of favorable outcomes is 38%. If they require, additionally, that patients have not had a flareup requiring treatment within 2 years, the percentage of favorable outcomes is 16%. This latter number resembles the results of Robinson et al. (2004), discussed above.

The available evidence warrants the conclusion that a significant proportion of individuals diagnosed with schizophrenia achieve poor outcomes. Importantly, whether assessed over shorter (e.g., 5–10 years) or longer (i.e., 15 years and more) durations, the functional outcomes of most individuals with schizophrenia appear particularly impaired, a result that occurs even when optimal psychopharmacological treatment has been administered over the entire follow-up period. To improve the outcomes achieved by these individuals, it stands to reason that factors must be identified that are causative of the observed social and occupational dysfunction. These factors, then, might serve as targets of interventions designed explicitly to improve outcomes and quality of life for individuals diagnosed with schizophrenia.

COGNITIVE THERAPY OF SCHIZOPHRENIA

Antipsychotic medications, while efficacious, have important limitations: Many patients continue to experience distressing residual symptoms despite taking appropriate doses, and, as we have seen, several of the most disabling features of schizophrenia are relatively unaffected by the medications (neg-

ative symptoms, functional impairment, and poor neurocognitive performance). These limitations, combined with the poor quality of life of most individuals with schizophrenia, led to the development of cognitive therapy as an adjunctive treatment for individuals diagnosed with schizophrenia (Chadwick et al., 1996; Fowler et al., 1995; Kingdon & Turkington, 1994). While this approach to schizophrenia shows the influence of early psychiatric pioneers such as Adolph Meyer, Henry Stack Sullivan, and Sylvano Areti, larger and more proximal influences are Beck's model of depression (Beck et al., 1979) and David Clark's approach to anxiety disorders (1986). In this section, we first consider the evidence base that has emerged, largely in the United Kingdom, in support of cognitive therapy for schizophrenia. Next, we briefly sketch the cognitive formulation and therapy for each of the major symptoms of schizophrenia that we will describe in greater detail in this volume.

Efficacy Research

Review of Reviews

Over the past 15 years an evidence base has accrued supporting the efficacy of cognitive therapy for individuals diagnosed with schizophrenia and schizoaffective disorder (Gould, Mueser, Bolton, Mays, & Goff, 2001; Pilling et al., 2002; Rector & Beck, 2001). In a recent quantitative review of 13 randomized controlled trials involving 1,484 patients, Zimmermann, Favrod, Trieu, and Pomini (2005) conclude that cognitive therapy confers, on average, compared to control treatments, 0.33 of a standard deviation more symptom reduction for patients in the chronic phase of schizophrenia, 0.5 of a standard deviation more improvement in psychotic symptoms during acute inpatient application, and 0.33 of a standard deviation more improvement across posttreatment follow-up periods. Cognitive therapy produces enduring changes in the positive symptoms of schizophrenia. By 2007, more than three dozen outcome trials had been published on cognitive therapy for schizophrenia.

Standout Studies

Perhaps the best study published to date was conducted by Sensky and colleagues (2000). In a single-blind, randomized controlled trial, cognitive therapy was compared to an active control treatment that was termed *befriending*. The results show that psychotherapy contact produces improvement in patients with schizophrenia, as both treatments produced significant and

equal changes in symptoms at the end of 9 months of active treatment. However, the results also illustrate that psychotherapy must confer skills to produce enduring change, as the patients treated with cognitive therapy maintained or improved upon their gains from baseline over the 9-month follow-up period, while the befriending-treated patients lost their gains and returned, as a group, to baseline levels of symptomatology. Indeed, patients treated with cognitive therapy had significantly lower negative symptoms for a full 5 years after treatment was completed (Turkington et al., 2008), evidencing considerable durability of treatment gains with regard to a symptom domain that has defied traditional treatment.

In the Sensky et al. (2000) trial, negative symptoms were not the focus of treatment. However, one of us (N. R.) has shown that important treatment gains can be achieved when negative symptoms are targeted directly by cognitive therapy (Rector, Seeman, & Segal, 2003). As compared to an enriched treatment-as-usual condition, patients treated with cognitive therapy showed improvement in negative symptoms over a 9-month follow-up period. Andrew Gumly and colleagues have shown that cognitive therapy can, additionally, reduce the likelihood of psychotic relapse effectively: Adding cognitive therapy to treatment as usual resulted in a 50% reduction in the relapse rate over a 12-month period (Gumley et al., 2003). Finally, a team lead by Tony Morrison at the University of Manchester has demonstrated that cognitive therapy can delay or reduce the onset of schizophrenia in individuals assessed to have "ultra-high" risk for developing schizophrenia. Morrison's group reported that 6% (2 of 35) of high-risk individuals treated with cognitive therapy developed a psychotic disorder over a 12-month period, as compared to 26% (6 of 25) in the nontreatment group (Morrison, French, et al., 2004). Cognitive therapy, additionally, is well tolerated; less than a quarter of high-risk participants dropped out of treatment. This finding is especially notable given the tolerability, ethical difficulties, as well as unsatisfactory results of antipsychotic medications in the prevention of schizophrenia (McGlashan et al., 2006).

Literature's Limitations

As the foregoing review illustrates, cognitive therapy is clearly a promising treatment for schizophrenia. However, we believe that it is important to point out that there is considerable room for improvement of the treatment. For example, most of the literature and theorizing has focused upon medicated outpatients experiencing residual psychotic symptoms. Negative symptoms have rarely been targeted, and patients with thought disorder have tended to be screened out of the clinical trials. Also, the assessment

of whether cognitive therapy can produce reductions in symptoms in individuals who refuse or cannot tolerate antipsychotic medications awaits systematic study. A related concern involves the flexibility of the existing protocols. Most of the studies (e.g., Kuipers et al., 1997; Sensky et al., 2000; Tarrier et al., 1998) involve a mean number of 20 sessions delivered over a 6- to 9-month period. Given the diversity of both symptom presentation and course in individuals with schizophrenia, we suspect that the existing protocols will work best for a subset of the patients, and, further, that more sessions delivered more often might be warranted for more severe patients. In this regard, we acknowledge the work of Robert DeRubeis and Steve Hollon, who report finding significantly improved rates of remission when medicines and cognitive therapy are combined to treat major depression over the course of a year (Hollon, 2007). Anecdotally, Turkington has reported successfully treating entrenched delusions with cognitive therapy delivered over a 12-month period, a pattern that we have observed in some of our patients, as well.

Cognitive Approach to Schizophrenia

Despite these limitations, cognitive therapy is a promising intervention in the treatment of schizophrenia. The present section introduces the cognitive approach that we take to schizophrenia in the present volume. The discussion follows the four primary symptom categories that comprise schizophrenia: delusions, hallucinations, negative symptoms, and formal thought disorder. For each symptom type, the cognitive formulation is described, and then a sketch of the therapy is outlined.

A few general principles can be articulated at the outset. First, we have found that the recovery model works best. We collaborate on setting long-term goals with the patients, which generally fall into three categories: forming relationships, getting a job or returning to school, and living independently. When delusions or hallucinations interfere with these goals, we deal with them directly. Second, in most cases of patients experiencing prominent delusions and hallucinations, we find that we do have to use our cognitive techniques to reduce the distress. Third, in adapting the general formulation for an individual patient, we need to have a conceptual formulation based on the patient's symptomatology, history, and neurocognitive functioning. Patients with a good premorbid history and a higher level of functioning can be approached with some of the usual cognitive techniques; those with significant neurocognitive impairment are treated somewhat differently. In those cases, the therapist is far more directive and

needs to spend considerably more time engaging the patient in individual sessions and providing explanations in fairly simple terms that the patient can remember.

Delusions

As defining characteristics of schizophrenia, delusions are beliefs that produce considerable distress and behavioral dysfunction in individuals with schizophrenia, often resulting in hospitalization. Factors that distinguish delusions from nondysfunctional beliefs (Hole et al., 1979) include how much the person's moment-to-moment stream of consciousness is controlled by the belief (pervasiveness), how sure the patient is that the belief is true (conviction), how important the belief is in the patient's meaning system (significance), and how impervious the belief is to logic, reason, and counterevidence (inflexibility, self-certainty). In Chapter 3, we present a cognitive model of delusions formulated within a phenomenological analysis of the characteristics and development of delusions. Cardinal features of the model are information-processing biases (e.g., egocentricity, externalizing bias, poor reality testing) and antecedent belief systems (e.g., self as weak and others as strong) that we propose may, in tandem, enhance psychological vulnerability for the development of paranoia and delusions. We apply the model to persecutory and grandiose delusions, as well as delusions of being controlled. This cognitive framework provides an understanding of delusions in terms cognitive distortions, dysfunctional beliefs, and attentional biases that are amenable to cognitive therapeutic interventions. Chapter 9, building on the formulation of Chapter 3, describes the assessment and therapy of the delusions of schizophrenia. Primary assessment foci include developing an understanding of the development of the delusional beliefs, specifying the supporting evidence, and determining the degree of moment-to-moment distress. Techniques are then marshaled to question the supporting evidence and test out adaptive alternative explanations. A final phase of the treatment entails addressing nondelusional cognitive schemas that render patients vulnerable to recurrence and relapse.

Hallucinations

Typically defined as perceptual experiences in the absence of external stimulation, hallucinations can occur in any sensory modality. Hallucinations occur during the waking state and are involuntary. The experience

of hallucination is not, of necessity, pathological, as the beliefs about their origin (i.e., my own mind vs. a computer chip) distinguish "normal" from abnormal. Auditory hallucinations are diagnostically the most significant modality and have, accordingly, been the subject of considerable theory and research. In Chapter 4, we present a cognitive framework that explains the most vexing questions regarding auditory hallucinations: How does the hallucinator come to hear his or her own thoughts in a voice other than his or her own? Why is the content of hallucinations primarily negative? Why do patients tend to attribute the hallucinations to an external source? Building on biological constructs, the cognitive formulation characterizes hallucination-prone patients as liable, in the face of isolation, fatigue, or stress, to experience involuntary auditory imagery. Primary mental candidates for this process of perceptualizing are emotion-laden or "hot" cognitions such as negative automatic thoughts (e.g., "I'm a loser"). We propose, additionally, that information-processing biases, especially a propensity to externalizing, lead to the development of dysfunctional beliefs about the "voice" experiences that reinforce the sense of the external origin. Patient beliefs that the "voices" are omnipotent, uncontrollable, and externally generated drive both the experience of distress and their behavioral appeasement strategies. Thus, a combination of dysfunctional beliefs and poor coping behaviors maintain auditory hallucinations. Chapter 10 presents cognitive-behavioral strategies, rooted in the formulation of Chapter 4, designed to reduce the distress and neutralize the behavioral impact of auditory hallucinations. The patient is encouraged to develop distance from the "voices" and to question inaccurate "voice" statements. Delusional and dysfunctional beliefs about the voice are elicited and questioned, as well, via behavioral experiments. Specifically, the patient comes to see that he or she has control over the voice, an efficacy that undermines much of the cognitive structure supporting emotional and behavioral reactions. As with the treatment of delusions, maladaptive, nondelusional beliefs such as those that result in a sense of worthlessness and powerlessness, which determine much of the distressing "voice" content, are elicited, tested, and replaced with more adaptive beliefs.

Negative Symptoms

The negative symptoms of schizophrenia—including reduced verbal (alogia) and nonverbal expressivity (affective flattening), as well as limited engagement in constructive (avolition), pleasurable (anhedonia), and social (asociality) activity—respond poorly to antipsychotic treatment and are,

accordingly, associated with considerable disability. Putting the existing research literature together with clinical examples, Chapter 5 describes a cognitive model of negative symptoms. Our approach emphasizes the process by which neurobiological challenges, such as those indexed by cognitive impairment, can, in turn, give rise to cognitive content, in the form of dysfunctional beliefs, negative expectancies, and pessimistic self-appraisals, that precipitate and maintain withdrawal from meaningful endeavors and diminish quality of life. Specifically, we propose that social-aversion beliefs, defeatist beliefs regarding performance, negative expectancies regarding pleasure and success, as well as self-stigmatizing illness beliefs and the perception of limited cognitive resources can all contribute to the negative symptoms of schizophrenia. Given that negative symptoms can arise from varying causes, assessment is a critical first phase of the treatment, described in Chapter 11. Negative symptoms that are found to be secondary to positive symptoms (e.g., not going outside because others will hear the "voices") will resolve by addressing beliefs related to the root cause. More generally, the therapeutic effort has two goals with regard to negative symptoms: (1) Help patients develop resources and enthusiasm for engaging in social, vocational, pleasurable, and other meaningful activity; and (2) guide patients to determine what sorts of factors lead them to disengage and then to develop less disruptive coping strategies. Because many patients with negative symptoms also have cognitive impairment, a variety of additional aids needs to be utilized, such as the hand-held computer to remind the patient of therapy-based homework assignments (e.g., going to bed at a reasonable time, engaging in social activities). In helping patients with predominant negative symptoms, we advocate abandoning Socratic questioning in favor of declarative statements made in definite, concrete terms, such as "Tell me what was upsetting during the past week" rather than "What was upsetting during the past week?" In addition to the memory aids, we enlist the family as a way of reinforcing our general approach in the homework assignments and reducing conflict and misunderstandings.

Formal Thought Disorder

Comprising a subset of the language disturbance found in individuals with schizophrenia, formal thought disorder can present considerable communicative challenge to individuals with schizophrenia and their interlocutors. Positive formal thought disorder, on the one hand, includes loosening of associations (various forms of getting offtrack in conversation as well as tangential responses) and idiosyncratic language use—neologisms (creat-

ing new words) and word approximations (employing actual words in a novel manner)—whereas negative thought disorder symptoms, on the other hand, consist of blocking (interruption in the flow of ideas), poverty of speech (conversation is restricted and responses often unelaborated), and poverty of content (normal flow of ideas with a reduced range of denotation). In Chapter 6 we develop a cognitive model of formal thought disorder that takes as its starting point the observation that speech becomes more disordered as patients prone to thought disorder experience stress. Seen in this light, thought disorder becomes, analogous to stuttering, a stress response to "hot" topics and situations. Because the patients have cognitive impairment, they have limited cognitive resources. Specific thoughts (e.g., "they will think I am stupid") triggered by particular situations sap these resources, exacerbating communicative difficulty. The patient develops defeatist beliefs regarding interlocutory efficacy, as well as a general sense of social aversion—cognitive structures that lead to avoidance of social situations and increased stress when such situations are encountered. In Chapter 12 we delineate the treatment approach for thought disorder based on the cognitive model. After an assessment of the topics that lead to thought disorder, the therapeutic interaction can be used as an opportunity to demonstrate to the patient that he or she can be understood. Later the relationship between stress and thought disorder can be illustrated, and beliefs regarding communicative efficacy elicited, tested, and modified.

Integrative Model

In addition to chapters detailing conceptualization and therapy for the four symptom categories, chapters focus on neurobiology (Chapter 2), general assessment issues (Chapter 7), creation and maintenance of engagement in therapy (Chapter 8), and collaborative pharmacotherapy (Chapter 13). The final chapter presents an integrative model of schizophrenia that pulls together concepts from the chapter on neurobiology and the conceptualization chapters (Chapters 3–6). The model features cognitive impairment and moves beyond domain-specific deficits to consider the global integrative capacity of the brain as a means to describe the genesis of schizophrenia. Stress and cognitive insufficiency combine to set up a hyperactivation of dysfunctional schemas and resource sparing that lead to the early negative symptoms that precede psychosis, as well as the reduced reality testing of florid psychosis and the semantic fragmentation of formal thought disorder. Dysfunctional beliefs and assumptions implicated in the development and maintenance of the three symptom dimensions are, moreover, targets

for therapeutic interventions (Chapters 9–12). By activating alternate networks and brain structures, cognitive therapy, we propose, helps patients tap into their cognitive reserve to reduce distressing symptomatology and other factors that impede goal-oriented activity and the achievement of an improved quality of life.

SUMMARY

In this chapter we have introduced the concept of schizophrenia, reviewed the essential historical context, painting a thumbnail sketch of the currently known facts, and considered the development of cognitive therapy in the context of antipsychotic treatment and outcome research. Additionally, the cognitive approach to schizophrenia was introduced and described for each of the major symptom dimensions of schizophrenia.

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