The voices arrived without warning on an October night in 1962, when I was fourteen years old. Kill yourself... Set yourself afire, they said. Only moments before, I’d been listening to a musical group called Frankie Valli and the Four Seasons singing “Walk like a man, fast as I can...” on the small radio that sat on the night table beside my bed. But the terrible words that I heard now were not the lyrics to that song. I stirred, thinking I was having a nightmare, but I wasn’t asleep; and the voices—low and insistent, taunting and ridiculing—continued to speak to me from the radio. Hang yourself, they told me. The world will be better off. You’re no good, no good at all.

After a time I began to hate work, and Bruce sometimes got on my nerves. I got depressed and crashed out of an evening, staying up all night listening to Pink Floyd’s “The Wall.” One day I was at work, Bruce was out and the phone rang. I picked it up. “We are following your every move,” said a voice; then nothing. Instantly the PA system from the next factory, which was quite loud, said, “Telephone for did-you-get-that? Telephone call for we-know-you’re-listening.”


At the beginning of that summer, I felt well, a happy healthy girl—I thought—with a normal head and heart. By summer’s end, I was sick, without any clear idea of what was happening to me or why. And as the Voices evolved into a full-scale illness, one that I only later learned was called schizophrenia, it snatched from me my tranquility, sometimes my self-possession, and very nearly my life.

I spent my junior year abroad. While I was in Spain my first semester, the Voices were softer, but I was so revved up, my motor seemed to be working overtime. When the Voices did speak to me, sometimes they did so in Spanish: “Puta! Puta!” they yelled. “Vaya con el diablo.” Go to hell, whore.

Along the way I have lost many things: the career I might have pursued, the husband I might have married, the children I might have had. During the years when my friends were marrying, having their babies and moving into houses I once dreamed of living in, I have been behind locked doors, battling the Voices who took over my life without even asking my permission.

Sometimes these Voices have been dormant. Sometimes they have been overwhelming. At times over the years they have nearly destroyed me. Many times over the years I was ready to give up, believing they had won.

Today this illness, these Voices, are still part of my life. But it is I who have won, not they. A wonderful new drug, caring therapists, the support and love of my family and my own fierce battle—that I know now will never end—have all combined in a nearly miraculous way to enable me to master the illness that once mastered me.

Today, nearly eighteen years after that terrifying summer, I have a job, a car, an apartment of my own. I am making friends and dating. I am teaching classes at the very hospital at which I was once a patient.

—From The Quiet Room, by Lori Schiller and Amanda Bennett. By permission of Grand Central Publishing. All rights reserved.

As is made clear in these personal accounts from those living with it, schizophrenia is one of the most debilitating of the mental disorders. In this chapter, I will introduce you to the nature of schizophrenia and its prevalence around the world. As such, you will learn about its symptoms and the time course of their development.
Schizophrenia Basics: Prevalence, Course, and Symptoms

Schizophrenia is part of a broad category of disorders referred to as schizophrenia spectrum and other psychotic disorders. Psychotic disorders (see Table 13.1) involve a loss of being in touch with reality and are characterized by abnormal thinking and sensory processes. Individuals with a psychotic disorder may show delusions, hallucinations, disorganized thinking and speech, abnormal motor behaviors, and negative symptoms. People with psychotic disorders other than schizophrenia may show psychotic symptoms for a brief period of time or for a longer duration. They may also show delusions, affective problems outside the normal range, or simply seem odd to those around them. Psychotic symptoms not part of schizophrenia can be induced through drugs, lack of sleep, and other medical conditions. Also, it should be noted that although the term schizophrenia comes from the Greek meaning to split the mind, it is a very different disorder from those of dissociation, such as dissociative identity disorder. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM–5; American Psychiatric Association, 2013) describes these conditions separately from schizophrenia. This chapter will focus on schizophrenia.

TABLE 13.1 Table of DSM–5 Schizophrenia Spectrum and Other Psychotic Disorders

<table>
<thead>
<tr>
<th>DSM–5 Diagnosis</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia</td>
<td>Symptoms such as delusions, hallucinations, disorganized thinking and speech,</td>
</tr>
<tr>
<td></td>
<td>abnormal motor behaviors, and negative symptoms, continuously present for at</td>
</tr>
<tr>
<td></td>
<td>least 6 months</td>
</tr>
<tr>
<td>Brief Psychotic Disorder</td>
<td>Symptoms such as delusions, hallucinations, disorganized thinking and speech,</td>
</tr>
<tr>
<td></td>
<td>abnormal motor behaviors, and negative symptoms lasting for less than a month</td>
</tr>
<tr>
<td>Schizophreniform Disorder</td>
<td>Symptoms such as delusions, hallucinations, disorganized thinking and speech,</td>
</tr>
<tr>
<td></td>
<td>abnormal motor behaviors, and negative symptoms lasting for at least 1 month but</td>
</tr>
<tr>
<td></td>
<td>less than 6 months</td>
</tr>
<tr>
<td>Schizoaffective Disorder</td>
<td>Symptoms such as delusions, hallucinations, disorganized thinking and speech,</td>
</tr>
<tr>
<td></td>
<td>abnormal motor behaviors, and negative symptoms along with those of a major</td>
</tr>
<tr>
<td></td>
<td>mood disorder (major depressive or manic)</td>
</tr>
<tr>
<td>Substance/Medication-Induced</td>
<td>Delusions or hallucinations related to drugs or medications</td>
</tr>
<tr>
<td>Psychotic Disorder Due to Another</td>
<td>Delusions or hallucinations related to a medical condition</td>
</tr>
<tr>
<td>Medical Condition</td>
<td></td>
</tr>
<tr>
<td>Catatonic Disorder Due to Another</td>
<td>Non-normal activity of the motor system such as stupor, holding of a posture,</td>
</tr>
<tr>
<td>Medical Condition</td>
<td>mutism, mannerisms, or grimacing</td>
</tr>
<tr>
<td>Unspecified Catatonia</td>
<td>Non-normal activity of the motor system such as stupor, holding of a posture,</td>
</tr>
<tr>
<td></td>
<td>mutism, mannerisms, or grimacing</td>
</tr>
<tr>
<td>Other Specified Schizophrenia Spectrum and Other Psychotic Disorder</td>
<td>Symptoms such as delusions, hallucinations, disorganized thinking and speech, abnormal motor behaviors, and negative symptoms that do not meet the criteria for other categories</td>
</tr>
<tr>
<td>Unspecific Schizophrenia Spectrum and Other Psychotic Disorder</td>
<td>Symptoms such as delusions, hallucinations, disorganized thinking and speech, abnormal motor behaviors, and negative symptoms that do not meet the criteria for other categories</td>
</tr>
<tr>
<td>Delusional Disorder</td>
<td>Presence of delusions for 1 month or longer without criteria for another</td>
</tr>
<tr>
<td></td>
<td>schizophrenia spectrum disorder</td>
</tr>
</tbody>
</table>
Schizophrenia affects one’s ability to express oneself clearly, to have close social relationships, to express positive emotions, and to plan for the future. Not everyone with schizophrenia displays the same symptoms. Individuals with schizophrenia may hear voices, see images not seen by others, believe that others wish to harm or control them, and have bizarre thoughts. The most common set of symptoms seen in individuals with schizophrenia over the past 100 years is a belief that others are out to get them and the hearing of voices that others do not hear (Insel, 2010).

Individuals with schizophrenia can display problems in terms of cognitive processes, emotional processes, and motor processes. Cognitive problems can be seen as a disorganization of thinking and behavior. In listening to a person with schizophrenia, you may note a speech style that although detailed does not seem to have a coherent focus and does seem to constantly change themes. Technically, these are referred to as *circumstantiality* and *tangentiality*. In more severe cases, the speech is actually incoherent and contains a stream of words that are unrelated to one another, which is referred to as *word salad*.

Mood symptoms include impairments in affective experience and expression. Depression is a common experience with schizophrenia along with thoughts of suicide. A number of individuals with schizophrenia hear voices that tell them to kill themselves. Ken Steele’s voices told him “Hang yourself. The world will be better off. You’re no good, no good at all” (Steele & Berman, 2001). Motor symptoms can range from repetitive behaviors such as rocking to total stiffness or lack of change in posture referred to as *catatonia*.

**Prevalence and Course of Schizophrenia**

Schizophrenia affects about 1% of the population. It is seen throughout the world with similar symptoms regardless of culture or geographical location. Onset of schizophrenia occurs in the late teens or early twenties. Males show an earlier onset than females by about 5 years. Some individuals with schizophrenia display the symptoms throughout their life. However, there is a subgroup of individuals who, a few years after the initial display of symptoms, show a lack of symptoms even without treatment (Jobe & Harrow, 2010). Even with symptoms, some people with schizophrenia are able to be part of the social and economic world experienced by healthy individuals. In fact, two of the individuals whose self-reports are included in this chapter work at major universities in the United States.

The symptoms of schizophrenia are not constantly present. There are examples of individuals with schizophrenia who were able to finish college and maintain jobs, even high-level jobs. Thus, individuals with schizophrenia may show periods in which they are able to function in terms of external realities. Symptoms for some people tend to appear in times of change or stress. Different individuals with schizophrenia may show very different symptoms. For example, some
individuals may hear voices but never see a visual hallucination. Others show a different presentation of symptoms. This has led some researchers to conclude that there exists a variety of similar disorders that are currently described by the term schizophrenia. This would suggest that schizophrenia is not a single disorder but a number of related disorders that are described by this term.

The course of schizophrenia generally first becomes evident in adolescence or young adulthood (Tandon, Nasrallah, & Keshavan, 2009). The course of the disorder is shown in Figure 13.1. The initial phase is referred to as the premorbid phase. During this phase, only subtle or nonspecific problems with cognition, motor, or social functioning can be detected. These are accompanied by poor academic achievement and social functioning. This is followed by a prodromal phase in which initial positive symptoms, along with declining functioning, can be seen. Based on prospective studies, this phase can last from a few months to years, with the mean duration being about 5 years. Next is the psychotic phase, where positive psychotic symptoms are apparent. For most individuals, this phase occurs at between 15 and 45 years of age, with the onset being about 5 years earlier in males than females. This phase is marked by repeated episodes of psychosis with remission in between. The greatest decline in functioning is generally seen during the first 5 years after the initial episode. This phase is followed by a stable phase characterized by fewer positive symptoms and an increase in negative ones (see definitions of positive and negative symptoms below). Stable cognitive and social deficits also characterize this phase. The actual course of the disorder varies greatly across individuals.

Individuals with schizophrenia tend to die earlier than those their age in the general population. These higher age-standardized mortality rates are approximately double those of the general population. The life span of individuals with schizophrenia is abbreviated by 15 to 20 years. Of those with this abbreviated life span, approximately 25% can be attributed to suicide and 10% to accidents. The remainder is related to medical conditions, particularly cardiovascular disease.

**Positive and Negative Symptoms**

Based on initial descriptions used by Hughlings Jackson in the 1800s, schizophrenia symptoms are referred to as positive or negative. The more familiar positive symptoms are hallucinations, delusions, disorganized thinking, and disorganized behavior. The more familiar negative symptoms include lack of affect in situations that call for it, poor motivation, and social withdrawal. Hughlings Jackson saw positive symptoms as reflecting a lack of high cortical control over more primitive brain processes. Negative symptoms, on the other hand, were the result of loss of function—what today we would refer to as a dysfunctional network of the brain. It should be noted that positive and negative are not evaluative terms when applied to symptoms of schizophrenia. Instead, they indicate either the presence of something unusual such as hearing voices or seeing hallucinations, which would be positive symptoms, or the lack of a normal human process, such as poor motivation or social withdrawal, which would be negative symptoms.
Elyn Saks Describes Her Day-to-Day Experiences With Schizophrenia

As you read about schizophrenia, you generally learn of the symptoms such as hearing voices or feeling that others are out to get you. What you don’t hear about is the way those with the disorder are successful. You also don’t often read about how an individual with schizophrenia lives her day-to-day life. In the following essay, Elyn Saks describes her experience of teaching a law school class.

My students filled the room. They were interested and eager, unusually so, given that they were second- and third-year law students for whom the fear and trembling that came with the first year had long since faded. The course was “Advanced Mental Health Law.” The day’s topic: Billie Boggs. A street person who lived over a hot air vent in midtown Manhattan, she threw food at people who wanted to help her and chased them across the street. Her rantings and ravings seemed crazy to most of the students, and we were discussing whether she should be sent to a psychiatric hospital.

I heard myself speak, surprising myself by the steady sound of my voice as I tried to restore my attention to the group before me: “What if Billie Boggs were your sister—would you put her in a psychiatric hospital then?” Up shot the hands.

Concentrate. These are your students. You have an obligation to them. Canceling class would be admitting defeat. But there are explosions in my head. They’re testing nuclear devices on my brain. They’re very little and they can get inside. They are powerful.

I pulled myself together, enough to point to a young woman who spoke often in class. “I couldn’t let my sister live like that,” she said from across the classroom, which held the students in curved rows, like a giant palm before me. “I know my sister. That wouldn’t be her. There’s one and only one of her—and that’s the one before she got sick.”

Is she trying to kill me? No, she’s a student. But what about the others? The voices inside my head, the explosions. What do they want? Are they trying to interdict me, to hit me with the Kramer device? I went to the store and they said “interdiction.” Interdiction, introduction, exposition, explosion. Voicemail is the issue.

I knew not to say those thoughts out loud. Not because they were crazy thoughts—they were every bit as real as the students sitting right in front of me—but I kept silent because others would think them crazy. People would think me as deranged as Billie Boggs.

But I’m not crazy. I simply have greater access to the truth.

“Good,” I replied. “But why isn’t it the case that your sister has two selves, the sick one you see now and the healthy one you’ve known all your life? Why should you get to pick which is real? Shouldn’t your sister make that choice?” Up shot more hands.

My brain is on fire! My head is going to explode right here, right in front of my class!

“But isn’t health always preferred to illness?” a bright-eyed young man countered. “We should prefer the healthy self.”

Mercifully, the class ended. A law-school dean spotted me as I walked back to my office. He said I looked as if I were in pain. “Just a lot on my mind,” I heard myself reply as I continued quickly down the hall. Keys out, door open, door shut. I crumpled into my chair and buried my face in my hands.

That was in September of 1991, and it was one of my worst such incidents. Ten years before, in my mid-20s, during my third psychiatric hospitalization, I had been given the diagnosis “chronic paranoid schizophrenia with acute exacerbation.” My prognosis? “Grave.” I was, in other words, expected to be unable to live independently, let alone work. At best I would be in a board-and-care, holding a minimum-wage job—perhaps flipping burgers—when my symptoms had become less severe.

That has not turned out to be my life. I am the Orrin B. Evans professor of law, psychology, and psychiatry and the behavioral sciences at the University of...
Southern California’s law school; adjunct professor of psychiatry at the University of California at San Diego’s medical school; and an assistant faculty member at the New Center for Psychoanalysis, where I am also a research clinical associate.

My schizophrenia has not gone away. I still become psychotic, as happened in class that day in 1991. Today my symptoms, while not as severe, still recur and I struggle to stay in the world, so to speak, doing my work. I have written about my illness in a memoir and much of the narrative takes place after I had accepted a tenure-track appointment at USC.

Barring a medical breakthrough of Nobel-Prize-winning proportions, I will never fully recover from schizophrenia. I will remain on antipsychotic medication and in talk therapy for the rest of my life. Yet I have learned to manage my illness.

There are steps that everyone with mental illness should take. First, learn about the illness you have—the typical signs, symptoms, and course. Many excellent sources are available. You may want to start with the Diagnostic and Statistical Manual of Mental Disorders, [DSM–5] Psychiatric textbooks, e.g., Kaplan and Sadock’s, can be helpful. I have also discovered excellent lay accounts of mental illness.

Second, understand how your illness affects you. What are your triggers? What are your early warning signs? What can you do to minimize your symptoms when they worsen—e.g., call your therapist, increase your medication, listen to music, exercise? Try to devise some techniques for your own situation. Some colleagues and I are studying how a group of high-functioning people with schizophrenia manage their symptoms. You are in the best position to determine what works for you.

Put a good treatment team in place. You need a therapist you can trust and can turn to in times of difficulty. Does he or she respond if you call in crisis?

The same is true of a psychopharmacologist. Make friends and family members part of your team.

Sometimes your team can see early warning signs before you can. For instance, my closest friend, Steve, and my husband, Will, often identify when I am slipping. Will says I become quieter in a particular way that signals all is not well. It’s a blessing to have such people in your life. Seek them out.

We also need to put a face on mental illness. Being open about one’s own illness will probably do more good than all the laws we can pass.

My own “outing” of myself was a bit of a risk, but has turned out well. I am glad and relieved I no longer have to hide. And my story seems to be meaningful to people—it has helped people understand mental illness more and perhaps has led to a decrease in the stigma. I was lucky in that my law school accommodated my teaching needs without my having to invoke the ADA. My colleagues are supportive, and I no longer feel ashamed about needing their help.

Perhaps most important: Seek help when you need it. Mental illness is a no-fault disease like any other, such as cancer or diabetes. Help is available, but you need to ask for it. Don’t let the threat of stigma deter you. You shouldn’t have to suffer.

And you shouldn’t allow mental illness to stand in the way of the wonderful contributions you are poised to make to your students and to your field.

Thought Question: What are the important components of Elyn Saks’s treatment plan? How do they apply to other psychological disorders?


Elyn R. Saks is a professor of law, psychology, and psychiatry and the behavioral sciences at the University of Southern California’s law school. She is the author of a memoir, The Center Cannot Hold: My Journey Through Madness (Hyperion, 2007).

Positive Symptoms

Hallucinations are sensory experiences that can involve any of the senses, although auditory hallucinations are the ones most commonly reported by individuals with schizophrenia. The two examples of hallucinations presented at the beginning of this chapter illustrate the unusual experiences that individuals with schizophrenia can have. Ken Steele, while listening to music on the radio, heard it tell him to kill himself. Richard McLean picked up a phone to hear voices tell him that they were following his every move. These auditory hallucinations were experienced as
coming from outside the person. Other individuals experience the voices or thoughts as coming from within their head. Individuals with schizophrenia report that they may hear voices throughout the day and on more than one day. Elyn Saks describes her experiences on a TED Talk in which she explains her thoughts during a psychotic episode and aspects of her treatment that helped her to improve (https://www.youtube.com/watch?v=f6CILJAA10Y). Her experience of giving a lecture at law school is related in the LENS: Elyn Saks Describes Her Day-to-Day Experiences With Schizophrenia.

Of course, all of us misinterpret our experiences once in a while. It is common for people to mistakenly believe that they heard someone call their name or that the phone rang while they were taking a shower. It is also common to mistake a stick on a path in the woods for a snake or to imagine an experience while falling asleep. These experiences are different from true hallucinations in that we check to see what the reality of the situation is or whether we are mistaken. Individuals with schizophrenia treat their hallucinations as real. In hallucinations in which individuals are instructed to perform an act, it is suggested that the instructions are obeyed by some 40% of people (Junginger, 1990). It should be noted that hallucinations can be produced by other disorders, such as Charles Bonnet syndrome, or the medications used to treat Parkinson’s disease. In these situations, the person experiences the hallucination but generally knows that it is not real.

Delusions are beliefs that have no support for their occurrence and are at odds with the individual’s current environment. One hospitalized patient believed that the CIA had cameras in the drawer pulls of her dresser. Elyn Saks, whose story was presented in the previous LENS, believed that powerful individuals could put thoughts in her head. John Hinckley, who tried to kill President Ronald Reagan, believed that Jodie Foster, the actress, would be impressed by this event. Another patient believed that God spoke to her when the dogs outside her house barked.

The most common delusions can be organized into categories. The first is persecution. This is the belief that other people or groups such as the CIA are plotting against the individual. John Nash (introduced at the beginning of Chapter 1) wrote letters to the U.S. government describing attempts of others to take over the world. The second category is grandeur. This is the belief that one is really a very famous person. The individual with schizophrenia may tell everyone that he is Jesus or some other famous figure. The third delusion is control. As in the case of Elyn Saks, the delusion is that someone or some entity such as aliens can put thoughts into one’s mind. A related delusion is that others can hear or understand one’s thoughts without being told what they are. Finally, one common delusion is that one is special and that God or important individuals are speaking directly to the person.

Long-term delusional activity varies with the individual. In one study, 43 individuals with schizophrenia were assessed six times over a 20-year period (Jobe & Harrow, 2010). Twenty-nine percent of those individuals had no delusional activity over that time, another 26% displayed delusions at each of the six assessments, and the remaining individuals had some delusions (see Figure 13.2).

**Negative Symptoms**

Negative symptoms seen in schizophrenia tend to be more constant and stable than positive symptoms. Several studies have linked negative symptoms with a poorer prognosis (see Foussias & Remington, 2010, for a review). Whereas it is usually the positive symptoms that result in a diagnosis of schizophrenia, it is the negative symptoms that tend to persist over time. Many individuals with schizophrenia have little interest in doing simple day-to-day activities such as taking a bath or
Chapter 13: Schizophrenia

shopping for food. This lack of will or volition is technically referred to as avolition. Individuals with schizophrenia also show a lack of interest in talking with others or answering questions with more than a one- or two-word answer. This is referred to as alogia. They also show a flattening of affect or difficulty expressing emotion. Another symptom is referred to as anhedonia or the inability to experience pleasure.

Multilevel Process for Diagnosing Schizophrenia

The text revision of the fourth edition of the DSM (DSM–IV–TR) and DSM–5 set forth a multilevel process for diagnosing schizophrenia.

The first level is symptoms, which includes delusions, hallucinations, or disorganized speech. At least one of these must be present. In addition, abnormal psychomotor behaviors, such as catatonia, and negative symptoms, such as a lack of volition or social processing, may also be present. The second level is functioning. A reduction in functioning in the areas of work, interpersonal relations, and/or self-care should be present. The third level is duration in which the presence of the positive or negative symptoms should have existed for 6 months with at least 1 month of positive symptoms. The final levels are designed to rule out psychotic-like symptoms found in other disorders such as mania or depression or those related to specific medical conditions such as drug abuse. The DSM–5 criteria are shown in Table 13.2.

Are There Subtypes of Schizophrenia?

Individuals with schizophrenia have a variety of different symptoms and exhibit an inconsistent picture of the disorder. This has led some to suggest that there is not a single schizophrenia disorder but rather a variety of syndromes. Historically, one approach to the variety of presentations seen in individuals with schizophrenia was to look for subtypes. As noted previously, Kraepelin suggested four subtypes. The fourth edition of the DSM divided schizophrenia into five subtypes. These are paranoid, disorganized, catatonic, undifferentiated, and residual subtypes. Although ICD-10 uses subtypes, DSM–5 removed the classification of subtypes but left the diagnostic criteria for schizophrenia almost identical to DSM–IV–TR. DSM–5 also uses the subtype descriptions

avolition: lack of will or volition
alogia: lack of interest in talking with others or answering questions with more than a one- or two-word answer
anhedonia: the inability to experience pleasure

FIGURE 13.2 Variations in Delusional Activity

Not all individuals with schizophrenia show long-term delusional activity. In this study, 29% had no delusional activity over the 20 years, another 26% displayed delusions at each of the six assessments, and the remaining individuals had some delusions. The figure shows the presence of delusional activity over a 20-year period for individuals with schizophrenia, other psychotic disorders, and others.

in classifying other psychotic disorders. I include the subtypes in this section since they are of historical importance and are currently used in ICD-10.

The paranoid subtype is characterized by delusions whose themes generally center on ideas of grandiosity or persecution. Individuals with this subtype might tell stories of how the FBI or CIA is out to get them and they must be constantly vigilant. Normal everyday occurrences such as seeing a person with a camera or encountering problems running a computer program would be interpreted as proof of the persecution. Others with the disorder might tell of how they have special powers, such as the ability to read someone’s mind. The criterion for being diagnosed with this subtype excludes disorganized speech, disorganized or catatonic behavior, or flat or inappropriate affect. Overall, these individuals show the greatest possibility of improvement.
The disorganized subtype, which was previously referred to as hebephrenic schizophrenia, is characterized by disorganized speech patterns and behavior. Individuals with this subtype display odd speech patterns often referred to as word salad in which a variety of words are put together in incoherent ways. Affective responses also appear odd to others in that little affect is shown in response to what should be significant events. Instead, silly or childlike responses are shown almost randomly. Whereas individuals with the paranoid subtype tend to have a consistent theme to their delusions, individuals with the disorganized subtype do not.

The catatonic subtype is characterized by non-normal activity of the motor system. One classic symptom is referred to as waxy flexibility in that the individual will remain in a fixed position. If someone moves the individual’s arms or legs, he or she will then remain in this new position. Motor movement can also be characterized by the opposite condition in which the individual shows excessive, purposeless activity of his or her motor system. Other possible manifestations of this subtype include the repeating of someone else’s speech, referred to as echolalia, and the repeating of someone else’s movements, referred to as echopraxia. Although these individuals may copy the speech or movements of others, they may not follow instructions and even refuse to speak.

Some researchers have suggested that catatonia should be considered a separate disorder and not part of the schizophrenia group (Fink, Shorter, & Taylor, 2010). Part of the support for this position is that these individuals do not respond as frequently to antipsychotic medication, and

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**Understanding Changes in DSM-5**

Since the 1800s, there have been constant debates concerning the nature of schizophrenia. Most researchers do not consider schizophrenia to be a single disorder, but rather a number of different disorders (Tandon, 2012). From this perspective, there are problems in determining exact criteria for schizophrenia.

With this in mind, a number of changes were made in DSM-5. First, two of five key symptoms are now required in DSM-5, for a diagnosis of schizophrenia, whereas DSM-IV required only one. These symptoms include (1) delusions, (2) hallucinations, (3) disorganized speech, (4) disorganized or catatonic behavior, and (5) negative symptoms. Second, DSM-5 requires that the individual have at least one of the most blatant symptoms: (1) delusions, (2) hallucinations, or (3) disorganized speech. Third, the subtypes such as paranoid, catatonic, undifferentiated, and so on, were removed.

The basic reason for dropping the subtypes from DSM-5 was that research has shown that these subtypes are not stable, and their differentiation is not supported by clinical evidence. Except for the paranoid and undifferentiated subtype, the others are rarely used in diagnoses. Fourth, a dimensional approach was introduced to rate the severity of the core symptoms of schizophrenia. This was established since different individuals with schizophrenia show different types of symptoms such as auditory or visual hallucinations.

Overall, there was less controversy with the change in the schizophrenia category in DSM-5 than with changes made in the diagnostic criteria for many other disorders. Some have been critical that DSM-5 did not rely more on neuroscience-based criteria. However, as shown in this chapter, an exact one-to-one relationship has yet to be established between brain measures of function, connections, chemistry, or structure and the presence of schizophrenia. Others see DSM-5 as a transition point toward the goal of basing criteria on neuroscience perspectives (e.g., Nemeroff et al., 2013). Finally, DSM-5 is also seen as a step toward bringing it and the newest version of ICD closer together on the criteria to be used in diagnosing schizophrenia (Tandon et al., 2013).
about 70% respond to the drug lorazepam alone. Lorazepam is a benzodiazepine associated with relaxation and is often given for treatment of anxiety disorders.

If an individual shows signs of schizophrenia but does not fit in any of the three major subtypes—paranoid, disorganized, or catatonic—then he or she would be diagnosed with an undifferentiated subtype.

A final subtype is referred to as the residual subtype. Individuals with this subtype have had schizophrenic episodes but no longer display the traditional positive symptoms of delusions and hallucinations. They may still display strange ideas or odd behaviors.

There has been considerable debate as to the value of using the five subtypes for diagnosis and treatment. Part of this debate involves a larger question of whether schizophrenia should be considered in terms of discrete categories or existing along a dimension. If schizophrenia exists along a dimension, then it would be meaningless to consider categories or subtypes (Linscott, Allardyce, & van Os, 2010). An additional question is whether the subtype information is actually used in making diagnoses and designing treatment. As noted, DSM–5 dropped the use of subtypes.

**CONCEPT CHECK**

- The symptoms of schizophrenia are characterized as positive symptoms and negative symptoms.
  - What is the definition of each symptom type?
  - What are primary examples of each type?
  - What role does each type play in the course of schizophrenia?
  - How are the four stages of the course of schizophrenia defined, and when do they typically occur? Is the course the same for each individual? If not, how does it differ?
  - What can we say about the prevalence of schizophrenia across the life span? Across genders?
  - The DSM has set forth a multilevel process for diagnosing schizophrenia. What are the characteristics of each of the levels?
  - What are the five subtypes of schizophrenia as defined by DSM–IV, and how are they characterized? How are they used in the current edition, DSM–5, and what led to the change?

**Historical and Evolutionary Perspectives on Schizophrenia**

As you will see in this section, schizophrenia has been described for thousands of years. As professionals began to study the disorder through case studies in the 1800s, different aspects were emphasized. As techniques from evolution and genetics were applied in the 1900s, it became apparent that schizophrenia is a very old disorder. In fact, schizophrenia was probably present when humans moved out of Africa some 100,000 years ago. As will be evident, genetics points to schizophrenia as a complex disorder that cannot be explained by single genes. A current focus of research is to discover underlying features of the disorder.

**Historical Perspective**

Disorders with psychotic-like symptoms have been described for at least 4,000 years (Tandon, 2012; Tandon et al., 2009; Woo & Keatinge, 2008). In addition, medical texts have been found throughout the ancient world that suggest that psychosis was present in all cultures. By the 1800s, the present-day terms of schizophrenia were being introduced. The German physician Ewald Hecker in the 1870s referred to a silly, undisciplined mind as Hebephrenia, named after the Greek goddess of youth and frivolity, Hebe. Figure 13.3 shows the evolution of the concept of schizophrenia.

In 1874, the German physician Karl Ludwig Kahlbaum used the terms paranoid and catatonic. Paranoid referred to the idea that someone felt himself or herself to be in danger.
Catatonic referred to the mannequin-like muscle stiffness associated with unusual postures. In 1878, Emil Kraepelin combined these various disorders into a single disease entity, which he termed dementia praecox or dementia of early onset. The word early referred to the fact that schizophrenia developed early in life rather than as part of a decline in mental functions associated with the dementias of old age. Overall, Kraepelin established what we now refer to as schizophrenia as a disorder with an onset in early adulthood that shows chronic and deteriorating progression and results in pervasive impairments in mental functions over the life span.

Kraepelin suggested there were four subtypes of dementia praecox. The first was the simple type, which was characterized by a slow decline along with social withdrawal and apathy. The second type was paranoid, characterized by fear of persecution. The third type was hebephrenic, characterized by a mania-like presentation. The fourth type was catatonic, characterized by a lack of movement. Kraepelin differentiated dementia praecox from what Falret in 1854 referred to as folie circulaire. Kraepelin referred to folie circulaire as manic–depressive insanity. Thus, Kraepelin established manic depression, which we refer to today as bipolar disorder, as a separate category from schizophrenia.

In 1911, Eugene Bleuler introduced the term schizophrenia, from the Greek meaning to split the mind. Bleuler was critical of the term dementia praecox and suggested that there was not a single schizophrenia but a number of different disorders or schizophrenias with different etiologies.
and prognoses. There were, however, a series of characteristics described by Bleuler often referred to as the four As.

1. **Affect**—Blunted or diminished emotional response
2. **Associations**—Loosening or inability to think in a logical manner
3. **Ambivalence**—Inability to make decisions
4. **Autism**—Social aloofness and an inability to remain in contact with the external world

These four As were thought to be unique to schizophrenia and present in those with the condition.

In the 1950s, the *DSM* was introduced and described psychosis in broad terms as a disorder resulting in serious functional impairment. Schizophrenia was differentiated from organic disorders such as neurocognitive disorders (dementia), which may produce psychotic behaviors. By *DSM–III*, schizophrenia was defined by more explicit criteria. In *DSM–IV* and *DSM–IV–TR*, the criteria for schizophrenia were broadened. This made the diagnostic criteria used in the United States with *DSM* and Europe with the *ICD* system more similar, thus reducing the differential diagnosis rates.

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**Case of James Stern**

**SCHIZOPHRENIA**

James Stern is a 20-year-old, single, Caucasian male who is a full-time student at a nearby university where he also works part-time to offset living expenses. He resides off campus with three roommates, and has been in an off-again, on-again relationship with his girlfriend since high school. He first sought treatment at a local student counseling center for anxiety, depression, and general distress at the urging of his family, but was then referred for longer-term individual psychotherapy due to the increasing severity of symptoms that were described by his therapist as paranoid ideation, ideas of reference, increasing distress, and dysphoric affect.

Mr. Stern confirmed that he had experienced symptoms that “others described as sounding paranoid” since high school, although he also reported that throughout his developmental years, he felt a lack of connection with his family and had few, if any, close friends throughout his primary and secondary school years. While he noted that he was always somewhat suspicious and guarded, he also reported that these feelings became much more intense after he relocated to the current local university from a much smaller college near his hometown. During this same time period, James also reported that he became increasingly reliant on the daily use of marijuana to ease/cope with associated symptoms of anxiety and distress. He was eventually “forced” to eliminate his usage because of his growing realization that the marijuana magnified feelings of paranoia that resulted in isolating himself in his room for days amidst a growing suspiciousness that his roommates and classmates had been infiltrated by “dark forces” that posed an increasing threat to mankind.

Following his cessation of marijuana use, James continued to struggle with perceptions that his professors were dropping surreptitious clues for him to decipher regarding the “dark forces” he still feared were infiltrating society, and he began to believe that those forces may have already “taken over” at least two of his roommates. At this point, his paranoia and fears about “evil forces” escalated rapidly, and he began to intermittently see “demons” moving among people. His distress elevated to the point that he refused to leave his apartment bedroom, which forced his withdrawal from school and termination of employment. Mr. Stern has been diagnosed with schizophrenia. Since beginning psychotherapy and pharmacotherapy, he has reported moderate to marked reductions in paranoia and distress, although he continues to report intermittent suspiciousness and ongoing uncertainty about his future in multiple domains (e.g., relationship, academic, and career goals).

Clinical vignette provided by Sandra Testa Michelson, PhD.
As noted earlier in this chapter, like DSM–IV–TR before it, DSM–5 includes a multilevel process for making a diagnosis of schizophrenia: symptoms, functioning, and duration. The case of James Stern (not his real name) illustrates difficulties in all three areas of functioning.

Evolutionary Perspective

There is an evolutionary paradox with schizophrenia (Huxley, Mayr, Osmond, & Hoffer, 1964)—individuals with schizophrenia have fewer children than others, and males with schizophrenia have even fewer children than females with schizophrenia. Given this situation, one would expect that the disorder would disappear over evolutionary time, and the genes of individuals with schizophrenia would not be passed on to the next generation. This, however, is not the case. How can the disorder exist without a reproductive advantage? A number of suggestions have been made. One is that the genes associated with schizophrenia are also associated with positive traits such as creativity, cognitive abilities, and language (Srinivasan et al., 2015).

It has been noted that many highly gifted and creative individuals manifest schizophrenic-like traits, referred to as schizotypal traits, without having the disorder. However, it is not uncommon for these individuals to have a first-degree relative with schizophrenia, suggesting a genetic component. Andreasen (2005) suggested there may be a connection with scientific creativity and schizophrenia within one's family. She noted that a number of Nobel laureates had family members who were thought to have schizophrenia, including Albert Einstein, Bertrand Russell, and John Nash. (As mentioned earlier, John Nash's story was described in the book and film \textit{A Beautiful Mind}.) But this still leaves open the question of how schizophrenia came about.

Two separate theories related to the evolutionary existence of schizophrenia were proposed by Tim Crow (2000) and Jonathan Burns (2004). Both of these theories note that schizophrenia is found throughout the world in approximately the same prevalence across cultures, and it is found in populations that have been separate from one another for at least 50,000 years. Since similar rates are seen in both industrialized and agrarian societies, this suggests that schizophrenia has existed as a part of the human experience since at least the time humans began migrations out of Africa some 100,000 years ago. If it were a newer disorder, then one would expect to find different rates in populations of humans in different parts of the world.

Tim Crow (2000) suggested that the development of language and the genetic changes required for producing and understanding speech were associated with the development of schizophrenia. Since the time of both Broca and Hughlings Jackson in the 1800s, it has been known that the brain is lateralized, with linguistic functions associated with left hemispheric networks. In 1879, Crichton-Browne suggested that since language processes evolved more recently than many other brain processes, these might be the first involved with mental disorders. Crow noted how one common positive symptom in schizophrenia around the world is the experience of hearing voices, which are experienced as separate from one's normal thought processes. This suggests a disruption in normal language processes resulting from incomplete differentiation of the hemispheres, leading to a loss of the ability to differentiate thought and speech. Crow and his colleagues (Angrilli et al., 2009), using electroencephalography (EEG), showed that individuals with schizophrenia compared with normal controls failed to show a left hemispheric dominance when processing language.

Jonathan Burns (2004) suggested that schizophrenia is better understood as a disorder of the social brain rather than of language ability. For Burns, schizophrenia results from disordered connections from the frontal to temporal areas and the frontal to parietal areas, which are critical brain connections related to social functioning. Historically, schizophrenia for Burns exists as the result of a trade-off at two separate stages of cognitive evolution in humans.

The first trade-off occurred between 2 and 16 million years ago. It was during this period that our species evolved specialized neural processing and complex interconnections of the brain required to respond to group living. To perform the tasks required for social living, a higher level
of cognitive functioning was required. In order for the brain to develop the circuits required, brain maturation was lengthened. That is, given the physical constraints of the developing brain in the human fetus, brain development time needed to be lengthened. This trade-off meant that the developing brain experienced a long period of time in which complex gene interactions or accidents could happen.

The second trade-off for Burns (2004) happened more recently, about 100,000 to 150,000 years ago. This date is important. Since schizophrenia is seen in all cultures with similar symptoms, it is assumed that the genes involved in its manifestation would have evolved before human groups began migrations out of Africa. What happened at this point was that some individuals experienced non-normal connections in the frontal areas of the brain. These connections resulted in some individuals being especially creative and thinking in different ways. These individuals may have been able to make important contributions to culture, much as our present-day artists and creative thinkers do. However, some individuals demonstrated a more severe version of these connections, which resulted in psychopathological experiences. Burns further suggested that this different way of experiencing the world in either its mild or severe form did not have any reproductive advantage. However, since the genes that controlled these experiences evolved as a part of the larger cortical networks needed for the cognitive and intellectual demands of social life, these genes continued to be passed on through their connections with adaptive mechanisms. Thus, according to Burns, schizophrenia represents one of the prices paid for evolving complex cognitive and social abilities. Further, it should be noted that ancient burial sites have bones of older individuals with various deformities. Since these individuals could not have survived without care from others, this suggests to some that individuals with schizophrenia-like symptoms may also have been cared for and made part of the community.

CONCEPT CHECK

• What can we say about the prevalence of schizophrenia across history? Across the world?
• “Disorders with psychotic-like symptoms have been described for at least 4,000 years.” Describe four important advancements in the development of the concept of schizophrenia since 1850.
• Describe the evolutionary paradox that schizophrenia presents. What different theories did Crow and Burns present to explain the paradox?

Factors in the Development of Schizophrenia

Schizophrenia typically is first noted during the transition from late adolescence to adulthood. However, theories related to its development generally see its onset at this time as the manifestation of a process that may have begun before the individual was born (Uhlhaas, 2011). In a review of birth cohort studies in which individuals are followed from birth, there is evidence to suggest that children who later develop schizophrenia show different profiles from those who do not (Welham, Isohanni, Jones, & McGrath, 2009). These data from seven different countries show subtle deficits in terms of behavioral disturbances, intellectual and language deficits, and early motor delays.

The current research literature suggests that schizophrenia is a disorder that begins early in life. This has led some researchers to suggest that we consider schizophrenia as a neurodevelopmental disorder (Insel, 2010). A variety of negative events can happen to a fetus including infections and malnutrition. It has been shown, for example, that vitamin D deficiency during pregnancy can be a risk for developing schizophrenia (McGrath, Burne, Féron, Mackay-Sim, & Eyles, 2010). Likewise, maternal infection is now regarded as a potential risk factor for schizophrenia (A. Brown & Patterson, 2011).

Overall, the theory that development of schizophrenia involves events experienced during pregnancy is referred to as the neurodevelopmental hypothesis. The basic idea is that during the time the fetus is in utero, an insult happens that influences the changes to the brain that later take place during adolescence.
Weinberger (1987) was one of the originators of the neurodevelopmental view and suggested that problems during the second trimester lead to an incomplete development of frontal lobe networks in the brain during adolescence. Currently, the neurodevelopmental hypothesis itself is not completely developed. However, the second trimester has clearly been noted as an important period in brain development.

What can be described about the reorganization of brain processes during adolescence in relation to schizophrenia? We know that adolescence is a time of great reorganization of cortical networks. Gogtay, Vyas, Testa, Wood, and Pantelis (2011) reviewed two longitudinal studies with this question in mind. The first data set was composed of individuals who developed schizophrenia before puberty and has been studied at the National Institute of Mental Health (NIMH). The second data set was from Melbourne, Australia, and included adolescents who are ultra-high risk for schizophrenia. Imaging studies showed larger ventricles and greater gray matter loss in the parietal and frontal areas in children who developed schizophrenia before puberty as compared with those who developed schizophrenia in adulthood. The data set from Australia indicated that those adolescents who developed schizophrenia showed greater gray matter loss, especially in the prefrontal cortex (PFC), as compared with those who did not develop the disorder.

Environmental factors can also play a role in the development of schizophrenia (van Os, Kenis, & Rutten, 2010). The basic idea is that environmental factors can influence the developing social brain and lead to the development of schizophrenia in those at risk. Such factors as early life adversity, growing up in an urban environment, and cannabis use have been associated with the development of schizophrenia. Being part of a particular ethnic group is not associated with schizophrenia per se, if the ethnic group lives together, but if one is a minority in a larger ethnic group, then there is an association. Also, if one moves from an urban environment to a rural one, then the chance of having schizophrenia goes down. Overall, greater amounts of stress are associated with greater chances of developing schizophrenia. However, environmental factors continue to reflect an interaction with genetic influences and are not a sole condition in themselves for developing schizophrenia (Sariaslan et al., 2016).

**Genetic Factors in Schizophrenia**

Since schizophrenia tends to run in families and is seen throughout the world, it is assumed to have a genetic component. That is to say, the risk of developing schizophrenia is much higher if someone else in your family also has the disorder. As can be seen in Figure 13.4, schizophrenia indeed has a strong genetic component. The more similar the genes between two individuals, one of whom has schizophrenia, the more likely the other person will also develop its characteristics. However, the genetic underpinnings of schizophrenia are not simple. It is clearly not the result of a single gene as with some other neurological disorders such as Huntington’s disease.

Research suggests that the number of genetic variants seen in individuals with schizophrenia is very large. There may be 1,000 different genes contributing to the disorder, which also include rare genetic variants (T. D. Cannon, 2015; E. Walker, Shapiro, Esterberg, & Trotman, 2010; Wray & Visscher, 2010). These genes may act in an additive or interactive manner to produce the disorder. In other words, there may be a variety of genetic combinations that are associated with schizophrenia. For example, heritable traits such as white matter connections and the thickness of gray matter in the brain are reduced in individuals with schizophrenia.

Those with schizophrenia show both fewer connections that link different parts of the brain and a reduction of dendrite connections at the level of the neuron. Adolescence and early adulthood bring extensive elimination of synapses in distributed association regions of the cerebral cortex, such as the prefrontal cortex. An impairment of this process takes place in those with schizophrenia. Research suggests that this is related to variations in the HMC locus, particularly...
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the genetic allele called component 4 (C4) (Sekar et al., 2016). This suggests that schizophrenia should be viewed as a developmental disorder that takes place as the brain is reorganized in adolescence.

Further, the genetic factors that influence the correlation between schizophrenia and white matter measures were found to be different from the genetic factors that influence the correlation between schizophrenia and reduced gray matter thickness (Bohlken et al., 2015). That is, there are different genetic pathways for each type of deficit.

In addition, individuals with schizophrenia compared with healthy controls show more abnormalities in their deoxyribonucleic acid (DNA) in the form of deletions or duplications of DNA sequences. Surprisingly, these gene abnormalities are even seen in the monozygotic (MZ) twin who does not develop schizophrenia as compared with the one who does. This suggests that these abnormalities are the result of both inherited and non-inherited factors.

If schizophrenia were a totally inherited disorder, then if one MZ twin developed the disorder, the other would also. However, this is not the case. There are three factors that may be playing a role in this situation. First, as genes are reproduced during fetal and later development, there may be slight changes in one twin as compared with the other. These are referred to as copy number variations. Maiti, Kumar, Castellani, O’Reilly, and Singh (2011) studied copy number variations in MZ twins from families with schizophrenia and found genetic differences in the twins. Thus, even identical twins can show differences in their total genetic makeup. Second, differences in twins may not result from differences in the DNA itself but from the results of epigenetic factors in which genes of an affected individual may be turned on differently from those of a non-affected individual, suggesting that internal and external environmental factors play a role (S. King, St-Hilaire, & Heidkamp, 2010). And third, environmental factors may play a role that does not involve genetic changes.

A number of studies over the years have shown that there is a higher concordance rate for MZ twins than for DZ twins. However, because of differences in how these studies were conducted in terms of diagnostic characteristics of schizophrenia, the concordance rates differ. Yet, in every study, MZ twins show a higher rate than DZ twins, supporting the importance of genetics. The initial studies of the 1990s show a 48% concordance rate for MZ twins. This suggests that the environment plays an important role. Although environmental stress is known to exacerbate the disorder, there is little evidence that psychological stress can actually cause schizophrenia. Further, adopted children from families with schizophrenia show a similar rate to those raised with their natural families. This implies that the manner in which individuals are reared is not directly related to the development of schizophrenia.

Other work has suggested a role for poor maternal nutrition or infections during fetal periods. However, this work is also inconclusive. A more recent review of the genetics of schizophrenia indicates a higher concordance rate for MZ twins and schizophrenia—82% (Rutter, 2006). Recent speculation suggests that epigenetics (see Chapter 2) may offer a more viable mechanism for the development of schizophrenia (Petronis, 2004).

Another way to examine the genetic factor is to look at adolescents whose parents had schizophrenia. When compared with healthy controls, adolescents who did not have schizophrenia but whose parents did were shown to have dysfunctional interactions within cortical networks involved in emotional processing (Diwadkar et al., 2012). This suggests an endophenotype could be connected with schizophrenia.

**Endophenotypes Associated With Schizophrenia**

Presently there is no one biomarker that can identify a person with schizophrenia. A number of researchers have sought to find endophenotypes related to schizophrenia (see Miller & Rockstroh, in press, for an overview). As described in Chapter 2, an endophenotype is a pattern of processes that lies between the gene (the genotype) and the manifestations of the gene in the external environment (the phenotype). These processes can be biological, such as white and gray matter integrity or patterns of EEG activity. They can also be a higher-level psychological process
such as difficulties with memory or difficulties in recognizing emotional changes or empathy. The only requirement is that there is a pathway from the gene to the endophenotype to the phenotype. In the case of psychopathology, the phenotype is typically the clinical expression of a disorder.

These stable internal physiological or psychological markers associated with schizophrenia have been found in a variety of areas. In one review of the literature, which compared individuals with schizophrenia, their relatives, and healthy control individuals, endophenotypes were found in five major areas (A. J. Allen, Griss, Folley, Hawkins, & Pearlson, 2009).

- The first area is **minor physical anomalies**, which include differences in head or body size or motor movements.
- The second area of **physiologic abnormalities** is based on the membrane theory of schizophrenia. This theory suggests that normal metabolism in the brain is disturbed in individuals with schizophrenia.
- The third area is **neuropsychological measures**. Studies reviewed in this area include such measures as the Wisconsin Card Sorting Test (WCST), in which the person must respond to changing demands, and the Continuous Performance Task, which measures attentional abilities.
- The fourth area involves **neuromotor abnormalities**. One task has to do with smooth pursuit eye movement. Individuals with schizophrenia show a different pattern of eye movement if asked to follow a person’s finger moving from right to left in front of them. Rather than showing a smooth motion of eye movement, they show periods of quick pursuit in which they attempt to catch up with the finger movement.
- The fifth area is **sensory processing and event-related potentials**. Numerous studies have shown EEG differences between individuals with schizophrenia and others. In response to cognitive tasks, the evoked potential waveforms of P50, P300, and N400 were noted as important.

As can be seen in Figure 13.4, individuals with schizophrenia and their first-degree relatives without schizophrenia show similar responses to tasks in the five areas. This suggests an endophenotype related to schizophrenia but not a definitive biomarker of the disorder.

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**FIGURE 13.4 Endophenotype Anomalies and Schizophrenia**

In terms of endophenotype anomalies, those with schizophrenia show the most, followed by their relatives, and the least are shown by healthy controls. This figure shows the average percentage abnormal for each endophenotype category for those with schizophrenia (SC), their relative (REL), and healthy controls (HC).

Source: Allen et al. (2009, p. 31). Used with permission from Elsevier.
Recent reviews of the literature suggest that cognitive deficits are among the most important symptoms of schizophrenia, especially in terms of their impact on society and quality of life (G. Miller & Rockstroh, in press). Factor analyses by Seidman et al. (2015) of data from 83 schizophrenia patients, 151 unaffected siblings, and 209 community comparison participants yielded five distinct cognitive factors. These factors are episodic memory, working memory, perceptual vigilance, inhibitory processing, and visual abstraction. Each of these factors was shown to be significantly heritable. Another review emphasizes the importance of social cognition in schizophrenia (Green, Horan, & Lee, 2015). Deficits in the ability to perceive social cues, regulate social emotions, and share with others are seen as potential endophenotypes related to schizophrenia. At this point, research studies are focused on determining appropriate biological and psychological endophenotypes related to schizophrenia, although a final list has yet to be determined.

In a series of papers, Rajiv Tandon and his colleagues (Tandon, 2012; Tandon et al., 2009; Tandon et al., 2013) reviewed the literature to determine what aspects of schizophrenia have been shown to be stable through a number of replications. These are presented in Table 13.3. These researchers also suggested that a dimensional approach including the study of endophenotypes will be important in future conceptualizations of schizophrenia.

### TABLE 13.3 Clinical “Facts” of Schizophrenia

- Schizophrenia is generally diagnosed on the basis of the presence of positive symptoms in conjunction with impaired social function in the absence of significant mood symptoms, other recognizable neurological illness, or substance use that can account for the psychotic symptoms.
- The nosological boundaries between schizophrenia and other psychiatric disorders are indistinct.
- There is significant heterogeneity in neurobiology, clinical manifestations, course, and treatment response across patients.
- Schizophrenia is characterized by an admixture of positive, negative, disorganization, cognitive, psychomotor, and mood symptoms.
- The severity of different symptom clusters varies across patients and through the course of the illness.
- There is a generalized but highly variable cognitive impairment.
- There may be additional specific impairment in a range of cognitive functions (such as executive functions, memory, psychomotor speed, attention, and social cognition).
- Cognitive impairments are present prior to onset of psychosis and persist during the course of the illness.
- There is a higher occurrence of obesity and cardiovascular disease.
- There is increased prevalence of cigarette smoking and other substance use disorders.
- There is increased suicidality.
- There is some phase-specific increase in violent behavior.
- There are significant premorbid impairments in a substantial proportion of patients.
- Onset of psychotic symptoms is usually during adolescence or early adulthood.
- The age of onset is earlier in males.
- There is an approximate doubling of age-standardized mortality.
- Schizophrenia is frequently a chronic and relapsing disorder with generally incomplete remissions.
- Social outcomes include reduced rates of employment and financial independence, and increased likelihood of homelessness and incarceration.
- Poor outcome is predicted by male gender, early age of onset, prolonged period of untreated illness, and severity of cognitive and negative symptoms.

Source: Adapted from Tandon et al. (2009). With permission from Elsevier.
CONCEPT CHECK

- Schizophrenia typically is first noted during the transition from late adolescence to adulthood, but current research suggests that the disorder begins early in life. What evidence from research into genetic and environmental factors points to this characterization?
- “Schizophrenia has a strong genetic component.” But it’s not simple and straightforward. What three factors that we’ve learned from research with MZ twins help to explain this genetic component?
- There is currently no one biomarker to identify an individual with schizophrenia. However, what five internal physiological or psychological markers associated with schizophrenia suggest a potential endophenotype related to schizophrenia?

Causes and Effects: Neuroscience

Findings About Schizophrenia

In this section, I will discuss structural and functional changes in the brain that are related to schizophrenia. This will include the manner in which chemical and electrical information moves throughout the brain. The section ends with a look at the cognitive changes found in schizophrenia. One of the more interesting phenomena seen in schizophrenia, which I will discuss at the end of this section, is the Charlie Chaplin illusion in which those with schizophrenia see a mask from an opposite perspective in comparison to those individuals without schizophrenia.

Schizophrenia and Brain Function

Schizophrenia manifests on a variety of levels including abnormal sensory experiences such as hallucinations, problems in cognitive processes such as delusions and disordered thought, changes in affect such as lack of expression, and in some cases problems with language and future directed planning. This presents a challenge to describe the manner in which brain processes relate to the disorder.

Current research examining individuals with schizophrenia has emphasized five different neuroscience measurements. The first is anatomical changes such as the loss of brain volume in particular areas. The second is functional processes such as the manner in which cortical areas and networks process information as seen in brain imaging. The third is neural oscillations that underlie the cortical networks. The fourth is changes in neurotransmitters such as dopamine, GABA, glycine, and glutamate. And the fifth is the development of cortical processes beginning in utero.

A variety of studies have shown that individuals with schizophrenia have emphasized differential activity in the dorsolateral prefrontal cortex (DLPFC), the ACC, and the thalamus (see Minzenberg, Laird, Thelen, Carter, & Glahn, 2009, for a meta-analysis). Due to its involvement with executive function tasks such as planning and social tasks, the frontal lobes have been extensively studied. When examining the entire brain and schizophrenia, other reviews point to enlargement of the ventricles and abnormalities of the medial temporal

RESEARCH TERMS TO KNOW

Factor Analysis

Factor analysis is a statistical technique that allows us to know which variables go together. Typically, a factor analysis study will collect a large number of variables on a group of individuals. The statistical technique creates factors that describe which of these variables are responded to in a similar way. For example, if a number of individuals were given a variety of cognitive tests, it is possible to see that those who do well on one type of problem also do well on another. One study found five factors related to intelligence. These were reasoning, spatial ability, memory, processing speed, and vocabulary (Deary, Penke, & Johnson, 2010). Another study examined psychopathology over 20 years in terms of personality functioning, life impairment, family histories and developmental histories of psychiatric disorders, and measures of brain integrity (Caspí et al., 2014). These researchers reported three factors. These were an internalizing liability related to depression and anxiety, an externalizing liability related to antisocial and substance-use disorders, and a thought disorder liability related to symptoms of psychosis.
lobe structures, including the amygdala, hippocampus, and neocortical temporal lobe functions (Shenton, Dickey, Frumin, & McCarley, 2001). More recent reviews point to a connection between the DLPFC and disorganized symptoms (Goghari, Sponheim, & MacDonald, 2010). In addition, the ventrolateral prefrontal cortex (VLPFC) was found to be associated with negative symptoms and the medial prefrontal activity with positive symptoms (see Figure 13.5).

The EEG reflects the electrical activity of the brain at the level of the synapse (Nunez & Srinivasan, 2006). It is the product of the changing excitatory and inhibitory currents at the synapse. The neural oscillations seen in the EEG offer a window for understanding how brain processes influence cortical networks, which can reflect normal cognitive, emotional, and motor processes. More low-frequency oscillations seen in the theta (4–7 Hz) and alpha (8–12 Hz) ranges reflect longer distant relationships in the brain, whereas higher frequency oscillations in the beta (13–30 Hz) and gamma (30–200 Hz) ranges reflect more local cortical networks (Uhlhaas & Singer, 2011, 2012).

Activity in the four frequency bands has been associated with a variety of cognitive processes in normal functioning. Since individuals with schizophrenia may show deficits in these cognitive processes, the study of cortical oscillations offers important insights into how schizophrenic processes affect the brain.

Cortical networks in the brain begin in utero and the period following birth. However, the development of these networks is not perfectly continuous. There is also a fundamental reorganization of these networks in adolescence (Uhlhaas et al., 2009; Uhlhaas & Singer, 2011, 2012). The reorganization during adolescence is reflected in both cognitive performance and EEG synchrony (Uhlhaas et al., 2009). Prior to adolescence, there is a period of increase over the years in both cognitive performance and EEG synchrony. This synchrony is reflected in similar EEG activity displayed in a variety of sites throughout the brain. However, during adolescence there is a decrease in both. After this period, there is a reorganization of EEG activity such that the synchrony is more focused at specific EEG sites, especially parietal and occipital electrodes.

Figure 13.6 depicts three critical periods in which changes in the physiology and anatomy of cortical processes would show changes consistent with the neurodevelopmental hypothesis of schizophrenia. The first period is fetal development in which genetic and epigenetic factors impair the electrical activity of the brain and with that the rhythmic activity associated with the formation of cortical circuits. Adverse experiences during fetal development are associated with the development of schizophrenia (Debnath, Venkatasubramanian, & Berk, 2015). The second stage involves the reorganization of cortical networks seen in adolescence. Along with this come changes in white and gray matter as well as neurotransmitters. Although all adolescents show gray matter declines in the PFC during this period of synaptic pruning, declines are higher in individuals with schizophrenia (Karlgodt, Sun, & Cannon, 2010). The third stage describes the situation in which individuals with schizophrenia fail to develop the coordinated networks necessary for normal cognitive processes.
According to current research, what are the five different neuroscience measurements related to individuals with schizophrenia?

What are the three critical periods of neurological changes in the development of schizophrenia?

What Brain Changes Are Seen in Schizophrenia?

Exactly when brain changes take place in those with schizophrenia is an important question. In order to better understand the role of timing in terms of brain structure, John Gilmore and his colleagues (2010) performed imaging studies before and after birth. These researchers used ultrasound scans prior to birth and magnetic resonance imaging (MRI) scans after birth while the babies slept. They compared children whose mothers had schizophrenia with a matched control group whose mothers did not have the disorder. Using ultrasound prior to birth, they found no differences between the two groups. After birth, males whose mothers had schizophrenia showed more gray matter in the brain, increased cerebrospinal fluid, and larger ventricles. Female infants did not show any differences. This suggests that at least the endophenotype for schizophrenia in males can be seen early in life.

Neuroimaging studies of those with schizophrenia have included both structural and functional approaches (Karlsgodt et al., 2010; Shenton & Turetsky, 2011). Structural approaches have focused on gray matter and white matter differences as well as the size of the ventricles (T. D. Cannon, 2015; Thompson et al., 2001). In a variety of reviews, both general and specific reductions in gray matter have been reported for individuals with schizophrenia. Specifically, reductions have been noted in the temporal cortex, especially the hippocampus, the frontal lobe, and the parietal lobe. In addition, the striatum part of the basal ganglia has been shown to be reduced.
**FIGURE 13.7  Gray Matter Reductions in Schizophrenia**

Even if they are identical (monozygotic, or MZ) twins, if one has schizophrenia there are gray matter reductions. This figure shows average gray matter deficit between identical twins. One twin has schizophrenia and the other does not. Note: Color represents the difference in gray matter between the twins.

Source: Cannon et al. (2001).

**FIGURE 13.8  Gray Matter Reductions After 5 Years**

Gray matter continue to decrease as schizophrenia develops. This figure shows early and late gray matter deficits in schizophrenia. Note: Color represents the difference in gray matter between individuals with schizophrenia and matched controls.


**FIGURE 13.9  Annual Loss of Gray Matter in Those With Schizophrenia**

As shown, gray matter loss is less in typical adolescents as compared to those with schizophrenia. Typical adolescents show around 1% or 2%, whereas those with schizophrenia show as much as 4% or 5% in some areas of the brain. The color represents percentage of gray loss.

Gray matter reductions have also been seen in cases when one identical twin has schizophrenia and the other does not (see Figure 13.7).

Since brain changes in chronic schizophrenia can be influenced by both the disorder itself and the medications that the individual has taken over a number of years, researchers have sought to determine gray matter changes in individuals who display their first episode of schizophrenia. These studies also suggest a reduction in gray matter in schizophrenia (Whitford, Kubicki, & Shenton, 2011). Further, similar reduction in gray matter was seen in a group of individuals who had been diagnosed with schizophrenia for an average of 21 years but had never received medications (Zhang et al., 2015). Overall, these studies rule out the possibility that brain volume reductions result from medication alone.

What might be at the heart of this gray matter reduction? One possibility is that the neurons actually die. However, a number of studies suggest this is not the case. What has been found is that the neurons in the brains of individuals with schizophrenia are more densely packed. This implies that the substance found between neurons—neuropil—was reduced, resulting in a greater density of neurons. Further, gray matter abnormalities have been shown to be partly hereditary and also related to trauma during pregnancy (Karlsgodt et al., 2010). Figure 13.8 shows the reduction of gray matter in the same set of individuals with schizophrenia over a 5-year period (Thompson et al., 2001). Figure 13.9 shows the differences in gray matter between individuals with schizophrenia and normal controls.

White matter changes have also been observed in individuals with schizophrenia. One study compared 114 individuals with schizophrenia with 138 matched controls in terms of white matter (White et al., 2011). Using a brain imaging technique—diffusion tensor imaging (DTI)—sensitive to white matter, individuals with chronic schizophrenia, individuals with first episode schizophrenia, and matched controls were compared. Figure 13.10 shows an example of tracking white matter through DTI. Measures of white matter were lower for individuals with chronic schizophrenia in the four lobes of the brain but not in the cerebellum or brain stem. Individuals experiencing their first episode of schizophrenia did not show significant differences from controls, which suggests that white matter reduction is part of the progression of the disorder over time.

In summary, gray matter and white matter changes in schizophrenia have been found in a large number of studies. In addition to white matter and gray matter changes in the brains of...
individuals with schizophrenia, researchers have sought to study cortical networks. I turn to this topic in more detail soon.

**Ventricle Changes in Schizophrenia**

There are four ventricles in the brain (see Figure 13.11). These ventricles contain cerebrospinal fluid. From a number of studies, individuals with schizophrenia show larger ventricles (see Vita, de Peri, Silenzi, & Dieci, 2006, for a meta-analysis). Since the walls of the ventricles are not rigid, it is assumed that larger ventricles result from a decrease in volume in other areas of the brain. Some of the other areas that have been shown to be smaller in individuals with schizophrenia are the frontotemporal cortices, the anterior cingulate cortex (ACC), and the right insular cortex.

One question is whether this reduction could be related to the medications that individuals with schizophrenia take. To answer this question, one study examined individuals with first episode schizophrenia and compared their brain structure with that of matched healthy controls (Rais et al., 2012). These researchers found brain volume loss in the individuals with schizophrenia. This suggests that the brain volume loss is present when symptoms begin. They found reduced volume in the temporal and insular cortex.

Figure 13.12 shows a larger ventricle in an MZ twin who had schizophrenia and a smaller one in the twin who did not.

**Schizophrenia and Brain Networks**

One common network studied in functional magnetic resonance imaging (fMRI) research is the default mode network (Raichle et al., 2001). This network is activated when individuals are not performing a task and letting their mind wander. The network involves both the frontal part of the brain (i.e., ventromedial prefrontal cortex [vmPFC]) and the posterior part of the brain (e.g., posterior cingulate, and the angular gyrus/inferior parietal lobe). Once an individual engages in a task, this network is suppressed and specific task-related networks become active.

In healthy individuals, greater suppression of the default network during a task is associated with better performance on that task (A. Kelly, Uddin, Biswal, Castellanos, & Milham, 2008). Individuals with schizophrenia and their first-degree relatives do not show the normal suppression of the default network when performing cognitive tasks (Whitfield-Gabrieli et al., 2009). Further, individuals who experience auditory hallucinations also show non-typical brain connections in the default network (Alderson-Day, McCarthy-Jones & Fernyhough, 2015). Individuals with schizophrenia also show weaker connections between brain areas than healthy controls, and the strength of connections is correlated with measures of memory, attention, and negative symptoms (Bassett, Nelson, Mueller, Camchong, & Lim, 2012).

Current brain imaging has allowed researchers to better identify cortical areas involved in hallucinations (P. Allen, Laroi, McGuire, & Aleman, 2008; Ford & Hoffman, 2013; Jardri & Sommer, 2013). It is suggested that in addition to sensory cortices, dysfunctions in prefrontal
premotor, cingulate, subcortical, and cerebellar regions also seem to contribute to hallucinatory experiences. One model suggests that a disruption in the information transfer from the left inferior frontal gyrus to Wernicke’s area contributes to the failure to perceive that inner experiences are actually coming from one’s self (Ford & Hoffman, 2013). That is, the person has the experience without knowing that it comes from his or her own brain.

Brain imaging research has suggested that individuals with schizophrenia show fewer connections between frontal and temporal areas of the brain while performing tasks. EEG measures offer one way of determining degree of connectivity. In a number of studies, Ford and her colleagues (e.g., Ford, Roach, Faustman, & Mathalon, 2007) have shown that individuals without schizophrenia show a cortical reduction of responsiveness to hearing their own voice talking, whereas those with schizophrenia do not. These researchers also reported that less connectivity between the frontal and temporal regions of the brain was seen when people with schizophrenia were talking versus individuals without schizophrenia (see Figure 13.13; Ford, Mathalon, Whitfield, Faustman, & Roth, 2002). Since there was even less connectivity in those individuals prone to hallucinate, this may be one mechanism involved in the mistaken experience that internal voices are produced externally (see also Fletcher & Frith, 2009).

**Neurotransmitters Involved in Schizophrenia**

There are certain neurotransmitters that are especially important in relation to schizophrenia (see Figure 13.14). The first is dopamine. It has been suggested that dopamine neurons are overactive in schizophrenia in midbrain areas and underactive in higher cortical areas (Abi-Dargham & Grace, 2011). These activations can in turn influence other brain areas with dopamine projections. This is referred to as the *dopamine imbalance hypothesis*. Supporting this hypothesis is the finding that there is a direct relationship between drugs that treat schizophrenia and their ability to bind to dopamine receptors in the brain. Further, stress not only increases symptoms in schizophrenia but also causes an activation of the hippocampus and an increase in dopamine activity.
On a broader level, creative ability in humans has been associated with dopamine functioning, especially in the thalamus. Specifically, decreased dopamine D2 receptor densities in the thalamus resulted in a lower gating threshold and thus increased information flow. This, in turn, could result in more creative thinking (Manzano, Cervenka, Karabanov, Farde, & Ullén, 2010).

Other researchers have suggested it is not the dopamine system per se that is involved in schizophrenia but that it is the result of other transmitters that regulate the dopamine system (Grace, 2010). This is supported by the fact that dopamine levels are not strongly elevated in schizophrenia. What is greater in individuals with schizophrenia is the induced release of dopamine by amphetamines. Further, the increased release is proportional to the ability of amphetamines to exacerbate psychosis.

The second neurotransmitter involved in schizophrenia is glutamate (Krystal & Moghaddam, 2011). Glutamate is an excitatory neurotransmitter in the brain. Further, another neurotransmitter, GABA (γ-aminobutyric acid), is involved in nearly all neuronal processes that engage the glutamate system. If the glutamate receptors in the brain are blocked in normal individuals, those individuals display psychotic-like symptoms.

At one time, the dopamine hypothesis and the glutamate hypothesis were seen as competing explanations involving the mechanisms of schizophrenia. Research has shown that giving substances that modify the activity of dopamine or glutamate could produce psychotic-like symptoms in healthy humans (Krystal et al., 2005). However, the type of psychotic presentation differed in terms of whether dopamine or glutamate receptors were affected.

How Are Cognitive Processes Changed in Schizophrenia?

Since cognitive tasks utilize specific cognitive networks, one approach to understanding the brains of individuals with schizophrenia is to note deficits in solving cognitive problems (Barch & Ceaser, 2012; Pearlson, 2011). Individuals with schizophrenia show cognitive deficits in a variety of cognitive domains, including executive function, working memory, and episodic memory. Overall, these cognitive processes all involve the DLPFC and its connections to other brain areas.
One suggestion is to develop a cognitive stress test similar to physical stress tests that determine the integrity of the heart. Two types of cognitive tasks that distinguish individuals with schizophrenia from healthy controls are those using working memory and those using attention. Working memory is the ability to keep information available for a short period of time, including its manipulation in planning and goal-directed behaviors. Disturbances in working memory are found in individuals with both acute and chronic schizophrenia as well as in their first-degree relatives without the disorder.

Imaging studies suggest the involvement of the DLPFC as well as the ACC, inferior parietal lobule, and hippocampus. The inferior parietal lobule is located just behind Wernicke’s area and is connected with large fiber tracts to both Broca’s and Wernicke’s areas. Overall, this area is associated with processing and integrating auditory, visual, and sensorimotor information. As suggested by DTI brain imaging measures, the problems seen with schizophrenia are probably better thought of as network problems rather than a deficit in a particular brain area.

One classic example of differential brain processing in individuals with schizophrenia is the Charlie Chaplin illusion. If healthy individuals look at a mask of Charlie Chaplin as it rotates, they will see the reverse side of the mask not as hollow but as convex. A video of the mask rotating can be seen at www.richardgregory.org/experiments. As you can see in the video, as the mask turns, an individual initially sees the hollow mask, but this changes into a normal face. Individuals with schizophrenia do not see the illusion and view the reverse side of the mask as hollow.

The Charlie Chaplin illusion has been studied with fMRI (Dima et al., 2009). What these researchers found was that individuals with schizophrenia and those without showed different types of connectivity in the brain. Specifically, individuals without schizophrenia showed more top-down processing when perceiving the illusion. This suggests that part of the illusion is the sensory expectation of how a face should appear. Thus, in healthy individuals, the brain creates the face as it should appear and not hollow as it actually is. Individuals with schizophrenia, on the other hand, show weakened top-down processes and stronger bottom-up ones. As a result, they see the sensory stimuli as they are without expectation. Overall, this is consistent with other research that suggests that individuals with schizophrenia lack the top-down expectations necessary to predict future events (e.g., P. Allen et al., 2008).

Individuals with schizophrenia may describe complex emotional processes when writing in a journal while at the same time showing limited emotional expression when interacting with others (Kring & Elis, 2013). Further, people with schizophrenia report similar emotional experiences as those without schizophrenia. However, individuals with schizophrenia do appear to have problems connecting emotions of others in a social situation with the context in which they occur. For example, in one study, those with schizophrenia as compared to control individuals showed less brain activity in the amygdala and visual cortex when shown faces of fear or happiness (Maher, Ekstrom, & Chen, 2015). Moreover, they tend to experience positive and neutral situations as more negative than those who do not have schizophrenia.
CONCEPT CHECK

- What structural brain changes in white matter and gray matter are characteristic of those with schizophrenia?
- Individuals with schizophrenia show larger ventricles in the brain. What do larger ventricles represent? When do they appear?
- What are the impacts of deficits in the brain’s default network and connectivity within and across networks in individuals with schizophrenia?
- “At one time, the dopamine hypothesis and the glutamate hypothesis were seen as competing explanations involving the mechanisms of schizophrenia.” What is the support for each hypothesis? What evidence suggests a more complex relationship?
- What is a cognitive stress test? What are three cognitive domains that show deficits in individuals with schizophrenia that would be the focus of the stress test?
- What are some of the problems in emotional processing experienced by individuals with schizophrenia?

Treating Individuals With Schizophrenia

Until about the 1960s, individuals with schizophrenia were placed in mental hospitals, often with little real treatment other than controlling them. With the advent of medications in the middle of the past century, it became possible for individuals with schizophrenia to live within community or home settings. In fact, individuals with schizophrenia tend to show more positive mental health behaviors when living within a community. In some cultures, small towns saw it as their duty to take care of these individuals. Today, after initial hospitalizations to gain control over symptoms, many individuals with schizophrenia return to their family. Other individuals continue their education or work. Some individuals, such as the ones noted at the beginning of this chapter, are able to be productive and succeed in high-level jobs with appropriate support. However, some individuals with schizophrenia become homeless and are at the mercy of their community. LEAVING: Mercy Bookings of Mental Patients describes how police around the United States try to protect these individuals.

FIGURE 13.15  Interventions Used at Each Stage of the Development of Schizophrenia

This figure shows the stages of schizophrenia and opportunities for intervention at each stage.

Source: From Tandon, 2012.
Over the past 100 years, there has been a shift in viewing schizophrenia as a disorder with inevitable deterioration to one in which recovery is possible (Frese, Knight, & Saks, 2009). Recovery includes having a career. Living with schizophrenia depends on the resources of the individual in terms of intellectual abilities, coping techniques, and willingness to accept the advice of professionals.

Treatment for schizophrenia involves addressing the specific stage of the illness. Figure 13.15 shows the major stages of the development of schizophrenia and some suggested treatment approaches at each stage. One major focus of treatment and research is the manner in which early intervention at each stage can reduce the severity of that stage. There are studies currently

**Thought Question:** What do you think are the pros and cons of mercy booking? What would you recommend as a consistent approach to community mental health treatment?
underway that are seeking to identify reliable indicators as to who will develop schizophrenia later in life (e.g., Cornblatt & Carrión, 2016). However, at this point the research is not definitive. Thus, knowing who should intervene and how remains a future possibility, although a number of programs are testing it out. Once signs of schizophrenia develop, early intervention becomes important. With signs of a psychotic episode, antipsychotic medication and psychological treatments are essential. Following this, supportive mechanisms such as family therapy and the creation of living and work conditions that help to reduce relapse are critical. I will discuss these approaches in more detail in this section of the chapter.

The Internet provides access to local and national groups that offer support for those with schizophrenia as well as their caregivers. In order to help individuals with schizophrenia cope in the community, a number of support procedures have been developed. These include antipsychotic medications as well as educational procedures to help the individual with schizophrenia and his or her family understand the course of the illness and the types of support available. As with other mental health disorders, specific psychotherapies for the person himself have been developed. Research suggests that the most effective treatment of schizophrenia should involve both medication and psychosocial approaches (A. T. Beck & Rector, 2005; Kane et al., 2016).

Antipsychotic Medications

A variety of medications have been used in the treatment of schizophrenia (Gopalakrishna, Ithman, & Lauriello, 2016; Hyman & Cohen, 2013; Kutscher, 2008; Minzenberg, Yoon, & Carter, 2010). The treatment of schizophrenia changed drastically in 1954 with the discovery of chlorpromazine (brand name Thorazine). When effective, this drug reduced agitation, hostility, and aggression. It also reduced the positive symptoms such as hallucinations and delusions and increased the time between hospitalizations associated with schizophrenia. However, negative symptoms and cognitive deficits were not changed by the drug.

One problem of this and other initial drugs were side effects such as **tardive dyskinesia**, which is a movement disorder that results in involuntary movement of the lower face and at times the limbs. These purposeless movements include sucking, smacking the lips, and making tongue movements. These and other movement side effects are difficult to reverse if the medication was given over a period of time. Weight gain is also seen with antipsychotic medications. In subsequent years, new and different classes of **neuroleptic** medications have been developed with different or fewer side effects (Gopalakrishna et al., 2016). These newer drugs tend to reduce the positive symptoms of schizophrenia such as hallucinations and delusions. They also help the individual think more clearly and remain calmer. Not all medications work for all individuals. There is also some suggestion that different ethnic groups respond differently to neuroleptics, although it is less clear whether it is genetic factors or diet that influences these differences.

Overall, medications for schizophrenia have been referred to as first-generation or second-generation antipsychotics. Second-generation antipsychotics are also known as **atypical antipsychotics**. First-generation antipsychotics influence dopamine receptors (D₂), although the exact mechanism by which they work is still being studied. One example of a first-generation antipsychotic medication is haloperidol, which has a number of trade names worldwide, one being Haldol. Second-generation or atypical antipsychotic medications influence the dopamine receptors differently. Both first- and second-generation antipsychotics are successful in treating the positive symptoms seen in schizophrenia. One advantage of the second-generation antipsychotics is that they are also able to treat the negative symptoms. Initially, it was thought that the second-generation antipsychotics had fewer motor side effects, but this has not always been shown to be the case (Peluso, Lewis, Barnes, & Jones, 2012). In fact, large-scale studies suggest that second-generation drugs are no more effective than the older ones (Hyman & Cohen, 2013).

One large-scale study of effectiveness of antipsychotic medication was conducted at 57 clinical sites in the United States in the early 2000s and involved almost 1,500 individuals with
schizophrenia (see Lieberman & Stroup, 2011, for an overview and update). This is referred to as the CATIE (Clinical Antipsychotic Trials of Intervention Effectiveness) study. Individuals with schizophrenia were randomly assigned to one of five antipsychotic medications (olanzapine [Zyprexa], quetiapine [Seroquel], risperidone [Risperdal], ziprasidone [Geodon], and perphenazine [Trilafon]) and followed for 18 months. An important aspect of the study was to compare first- and second-generation antipsychotic medications. One surprising result was that the second-generation medications did not show greater effectiveness than the first-generation medication, perphenazine. This included no greater effectiveness in terms of negative symptoms and cognitive impairment. These results had implications not only for treatment effectiveness, but also for economic considerations, since first-generation medications are less expensive. The CATIE study brought forth much controversy in the years following its publication (Lieberman & Stroup, 2011).

Psychosocial Interventions for Schizophrenia

Psychosocial factors play an important role in the overall treatment of individuals with schizophrenia. It has been estimated that over 60% of people with a first episode of a major mental illness return to live with relatives. Thus, families play an important role in supporting these individuals. In fact, family interventions for schizophrenia reduce relapse and hospitalizations. A number of meta-analyses looked at evidence supporting family interventions (see Barrowclough & Lobban, 2008, for an overview). In general, family interventions involve the following key components:

1. Provide practical emotional support to family members.
2. Provide information about schizophrenia, what mental health services are available in the community, and nationwide support services (such as those found on the Internet).
3. Help the family develop a model of schizophrenia (including not blaming themselves).
4. Modify beliefs about schizophrenia that are unhelpful or inaccurate.
5. Increase coping for all family members.
6. Enhance problem-solving skills.
7. Enhance positive communications.
8. Involve everyone in a relapse prevention plan.

A number of manuals involving cognitive behavioral therapy (CBT) approaches to schizophrenia are available (e.g., Kingdon & Turkington, 1994; L. Smith, Nathan, Juniper, Kingsep, & Lim, 2003). The basic model suggests that what is important is the manner in which individuals interpret psychotic phenomena (Beck & Rector, 2005; A. Morrison, 2008). The overall model suggests that neurocognitive impairment in the premorbid state makes the individual vulnerable to difficulties in school or work, which leads to nonfunctional beliefs such as “I am inferior,” maladaptive cognitive appraisals, and in turn nonfunctional behavior such as social withdrawal (Beck & Rector, 2005). The cognitive approach is aimed at helping the client understand the psychotic experience as well as cope with the experience and reduce distress. One key feature of schizophrenia is the disruption...
of thought processes, and one part of the treatment is directed at these illogical associations. Another focus of the treatment is directed at interpersonal relationships and success at work. This approach may also involve skills training such as self-monitoring and activity scheduling. Since individuals with schizophrenia may also show mood and anxiety problems, CBT aimed at these processes can also be utilized. The key features of CBT for schizophrenia can be summarized as follows (Beck & Rector, 2005; Turkington, Kingdon, & Weiden, 2006):

1. Develop a therapeutic alliance based on the client's perspective.
2. Understand the client's interpretation of past and present events.
3. Develop alternative explanations of schizophrenia symptoms.
4. Normalize and reduce the impact of positive and negative symptoms.
5. Educate the client in terms of the role of stress.
6. Teach the client about the cognitive model including the relationships between thoughts, feelings, and behaviors.
7. Offer alternatives to the medical model to address medication adherence.

Developing a therapeutic alliance, that is, a relationship between the therapist and client that helps the work of therapy, is an initial task of therapy. Part of this may include talking with the client about his delusional beliefs. For example, if a client says that he invented a machine to solve the world's problems, then the therapist might ask when the person had this idea and what he has done to create the machine. The therapist might also ask him about others who had helped him with his ideas. As with CBT for other disorders, the basic idea is to look for inconsistent thoughts and conclusions that do not follow logically. For example, if no one would help the person with his machine, it does not follow logically that everyone is out to get him.

Another major task of therapy is helping the individual develop an alternative understanding of his or her symptoms. For example, some individuals with schizophrenia experience the voices that they hear as coming from outside of them. One goal of therapy would be to help the client reinterpret the source of the voices. Part of this may also include a cognitive assessment of alternatives to obeying the voices.

The role of stress in increasing symptoms of schizophrenia is an important concept for clients to understand. It is also important for them to understand the problems associated with not taking medication to control the symptoms of schizophrenia. Keeping individuals with schizophrenia on their medications is a difficult problem. In studies involving active medication alone versus a placebo alone, the relapse rates are about one half with medication compared with a placebo (32% vs. 72%) (Hogarty & Goldberg, 1973). Based on current studies, treating individuals with schizophrenia with both CBT and psychotropic medication appears to be the most effective approach (see Beck & Rector, 2005, for outcome studies).

In the 1950s, George Brown in London, England, sought to understand why some individuals with schizophrenia were readmitted soon after their hospital discharge with their symptoms reoccurring (Brown, 1985). He discovered that one important factor was the emotional environment in the home. This came to be referred to as expressed emotion, which refers to the emotions that the person with schizophrenia would experience from others. That is, homes in which the person experienced critical comments, hostility, and angry arguments were associated with relapse, whereas homes with warmth and positive remarks were not. Since that time, a number of intervention programs have been developed involving caregivers and others who live with those with schizophrenia (Amaresha & Venkatasubramanian, 2012).

A new approach is being tried in the treatment of schizophrenia—early intervention (M. Fisher, Loewy, Hardy, Schlosser, & Vinogradov, 2013). This approach seeks out those who
Something new is happening in major corporations and institutions in this country. Successful individuals who have experienced such disorders as schizophrenia, depression, and bipolar disorder are forming networks to support and educate others. One of these is The Stability Network (http://www.thestabilitynetwork.org/). This particular network consists of over 30 individuals who will speak publicly about their mental health experiences. They are also successfully employed in all forms of employment. One of these people is Robert Boorstin who was a former director of public policy at Google. Another is Elyn Saks, whose experiences with schizophrenia are offered in the LENS: Elyn Saks Describes Her Day-to-Day Experiences With Schizophrenia. All of the people involved can describe their experiences and beliefs. One person thought she could walk on the Charles River in Boston when she was at the Harvard Business School. Another believed his hotel room was the Starship Enterprise. However, each has worked with professionals and developed routines for stabilizing his or her condition.

The Stability Network set as its goal the following:

- Successfully living with a mental health condition(s), such as depression, anxiety, schizophrenia, and bipolar disorder (per the National Alliance on Mental Illness definition).
- Willing to openly speak out about your mental health condition(s), using both your first and last name.
- Committed to taking individual and collective action to improve the lives of those living with mental health conditions.
- Committed to staying healthy.

We ask our leaders to make specific commitments to

- SHARE their stories.
- IMPROVE mental health in the workplace.
- RAISE funding for mental health.

We provide leaders with

- A NETWORK of peers to collaborate with on improving the lives of others with mental health conditions.
- SUPPORT to increase their impact.
- MECHANISMS for collective impact.

Mental health disorders often carry with them a stigma. However, psychological research tells us that actually meeting and talking with someone about his or her condition can change that stigma.

Thought Question: You've now read a lot of psychological research concerning mental health disorders: What specific actions would you recommend that your university or community take to reduce the stigma of psychological disorders?
Another new approach, referred to as NAVIGATE, has been designed for the treatment of first episode psychosis (Kane et al., 2016). NAVIGATE is a multidisciplinary, team-based approach that emphasizes low-dose antipsychotic medications, cognitive behavioral psychotherapy, family education and support, and vocational and educational support. The program also helps the person to engage in his or her community. One advantage of this approach is that the individual with first episode psychosis receives all of these different treatment approaches. In a randomized control study involving 34 community mental health centers in 21 U.S. states, the NAVIGATE program was shown to be more effective than the standard care found in the community health center. Further, the earlier the person entered treatment after the first psychotic episode, the better his or her outcome measures were. Based on these types of results, the National Institute of Mental Health has announced the Early Psychosis Intervention Network (EPINET) (http://www.nimh.nih.gov/concept-clearance/EPINET).

Many professionals involved in the treatment of schizophrenia have come to realize that people are more likely to accept treatment and follow directions if they are involved in their own treatment. A number of states have coordinated treatment approaches such as NAVIGATE that use a multidisciplinary team as well as input from the person with schizophrenia. This is critical, since many youth in the early stages of schizophrenia drop out of conventional medication-alone treatment.

**CONCEPT CHECK**

- What are three critical shifts in the past 60 years that have transformed the treatment of schizophrenia from institution-based to community-based?
- “Treatment for schizophrenia involves addressing the specific stage of the illness.” What specific treatments are suggested for different stages of the illness, and why?
- A variety of classes of medications have been used in the treatment of schizophrenia. What are they, and what are the advantages and disadvantages of each?
- What four psychosocial approaches are currently used in the treatment of individuals with schizophrenia, and what is the primary focus of each approach?

**SUMMARY**

Schizophrenia is one of the most debilitating of the mental disorders. It is part of a broad category of mental illness referred to as psychotic disorders, all of which involve a loss of being in touch with reality and problems with cognitive, emotional, and motor processes. Schizophrenia affects about 1% of the population. It is seen throughout the world with similar symptoms regardless of culture or geographical location. Onset of schizophrenia occurs in the late teens or early twenties. Males show an earlier onset than females by about 5 years. Symptoms are referred to as positive or negative. The more familiar positive symptoms are hallucinations, delusions, disorganized thinking, and disorganized behavior. The more familiar negative symptoms include lack of affect in situations that call for it, poor motivation, and social withdrawal. Not everyone with schizophrenia displays the same symptoms. This has led some researchers to suggest that there exist a variety of similar disorders that are currently described by the term *schizophrenia*.

Disorders with psychotic-like symptoms have been described for at least 4,000 years, and ancient medical texts suggest that psychosis was present in all cultures. The present-day concept of schizophrenia began to evolve in the middle of the 1800s. Beginning in the 1950s, the *DSM* was introduced and described psychosis in broad terms. By *DSM–III*, schizophrenia was defined by more explicit criteria, and in *DSM–IV* and *DSM–IV–TR*, the criteria for schizophrenia were broadened to become similar to the diagnostic criteria used by *ICD*. Most recently, the text revision of the fourth edition of *DSM* (*DSM–IV–TR*) and *DSM–5*...
set forth a multilevel process for diagnosing schizophrenia: (1) symptoms, (2) functioning, and (3) duration; the final levels are designed to rule out psychotic-like symptoms found in other disorders. Since individuals with schizophrenia have a variety of different symptoms and show an inconsistent presentation of the disorder, some have suggested that there is not a single schizophrenia disorder but rather a variety of syndromes. DSM–IV divided schizophrenia into five subtypes: paranoid, disorganized, catatonic, undifferentiated, and residual. There has been considerable debate as to the value of using the five subtypes due to the larger question of whether schizophrenia should be considered in terms of discrete categories or existing along a dimension. Although ICD-10 uses subtypes, DSM–5 removed the classification of subtypes but left the diagnostic criteria.

There is an evolutionary paradox with schizophrenia: How can the disorder exist without a reproductive advantage? One possible answer is that the genes associated with schizophrenia are also associated with positive traits such as creativity, since it has been noted that highly gifted and creative individuals manifest schizophrenic-like characteristics, referred to as schizotypal traits, without having the disorder. Other scientists propose different evolutionary paths: Crow theorizes that the development of language and the genetic changes required for producing and understanding speech were associated with the development of schizophrenia, while Burns suggests that schizophrenia is better understood as a disorder of the social brain rather than language.

Schizophrenia typically is first manifested during the transition from late adolescence to adulthood at a time of great reorganization of cortical networks. However, current research literature suggests that we consider schizophrenia as a neurodevelopmental disorder that begins early in life. The basic idea is that during the time the fetus is in utero, an insult happens that influences the changes to the brain that take place during adolescence. Schizophrenia has a strong genetic component; however, the genetic underpinnings of schizophrenia are not simple. The number of genetic variants seen in individuals with schizophrenia is very large, and these genes may act in an additive or interactive manner, leading to a variety of genetic combinations associated with schizophrenia. Genetic differences may result not from differences in the DNA itself but from epigenetic factors, suggesting internal and external environmental factors play a role. Finally, environmental factors that do not involve genetic changes may also play a role.

Presently, there is no one biomarker that can identify a person with schizophrenia. However, in comparing individuals with schizophrenia, their relatives, and healthy control individuals, endophenotypes have been found in six major areas: (1) minor physical anomalies, (2) physiologic abnormalities due to normal metabolism in the brain being disturbed, (3) neuropsychological measures, (4) neuromotor abnormalities, and (5) sensory processing and event-related potentials. Another physiological marker that distinguishes individuals with schizophrenia is larger ventricles in the brain resulting from a decrease in volume in other areas of the brain.

Schizophrenia manifests on a variety of levels including abnormal sensory experiences such as hallucinations, problems in cognitive processes such as delusions and disordered thought, changes in affect such as lack of expression, and in some cases problems with language and future directed planning. This presents a challenge to describe the manner in which brain processes relate to the disorder. Current research examining individuals with schizophrenia has emphasized five different levels of analysis from a neuroscience perspective. The first is anatomical changes such as the loss of brain volume in particular areas. The second is functional processes such as the manner in which cortical areas and networks process information as seen in brain imaging. The third is neural oscillations that underlie the cortical networks. The fourth is changes in neurotransmitters such as dopamine and glutamate. And the fifth is the development of cortical processes beginning in utero.

Until about the 1960s, individuals with schizophrenia were placed in mental hospitals, often with little real treatment other than controlling them. With the advent of medications in the middle of the last century, it became possible for individuals with schizophrenia to live within community or home settings. In fact, they tend to show more positive mental health behaviors when living within a community. In addition, over the past 100 years, there has been a shift in viewing schizophrenia as a disorder with inevitable deterioration to one in which recovery is possible. In order to help individuals with schizophrenia cope in the community, a number of support procedures have been developed. These include antipsychotic medications; educational procedures to help the individual with schizophrenia and his or her family to understand the course of the illness and the types of support available; and specific psychotherapies, particularly CBT approaches. Research suggests that the most effective treatment of schizophrenia should involve both medication and psychosocial approaches.
REVIEW QUESTIONS

1. This chapter states that “individuals with schizophrenia have a variety of different symptoms and show an inconsistent picture of the disorder. This has led some to suggest that there is not a single schizophrenia disorder but rather a variety of syndromes.” What do you think: Is schizophrenia one disorder? What evidence would you cite to support your position?

2. What are the environmental and genetic factors that play a role in the development of schizophrenia?

3. “Current research examining individuals with schizophrenia has emphasized five different levels of research from a neuroscience perspective.” For each type, what has been the focus of the research, and what brain changes have been found in schizophrenia?
   a. Anatomical changes
   b. Functional processes
   c. Neural oscillations
   d. Neurotransmitters
   e. Development of cortical processes

4. “Psychosocial factors play an important role in the overall treatment of individuals with schizophrenia.” What are the characteristics of each factor, and what role does each play in treatment?
   a. Family interventions
   b. CBT approach
   c. Early intervention

5. “Over the past 100 years, there has been a shift in viewing schizophrenia as a disorder with inevitable deterioration to one in which recovery is possible.” What impact does this shift suggest for changes in research, education, and public policy?

FOR FURTHER READING


KEY TERMS AND CONCEPTS

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<tr>
<th>allogia</th>
<th>disorganized subtype</th>
<th>psychotic disorders</th>
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<td>anhedonia</td>
<td>hallucinations</td>
<td>schizophrenia</td>
</tr>
<tr>
<td>avolition</td>
<td>negative symptoms</td>
<td>schizotypal traits</td>
</tr>
<tr>
<td>catatonic subtype</td>
<td>paranoid subtype</td>
<td></td>
</tr>
<tr>
<td>delusions</td>
<td>positive symptoms</td>
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13.1 Describe the prevalence of schizophrenia and the time course of its development.

13.2 Identify the positive and negative symptoms of schizophrenia.

13.3 Discuss the historical and evolutionary contexts of schizophrenia.

13.4 Identify genetic and environmental factors in the development of schizophrenia.

13.5 Describe the brain changes seen in individuals with schizophrenia.

13.6 Identify the treatments available to individuals with schizophrenia.